

**Decoupling Market Incumbency from Organizational Experience:  
A Study of Biotechnology's Impact on the Market for Anti-Cancer Drugs**

by

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## **Abstract**

In studies of creative destruction, scholars agree that, within research-intensive industries, the demise of incumbents is significantly determined by their lower productivity in researching the radically new technology (Henderson, 1993). Such differences in the research competence of incumbent vs. entrant firms are explained in the literature through theories about established vs. de novo firms (e.g., Nelson and Winter, 1982). A disconnect arises because, frequently, the most competent entrants are established (experienced) firms themselves (i.e., diversifying entrants). In fact, studies where diversifying and de novo entrants are compared find in the former the same mechanisms that scholars have argued take place in incumbent firms (e.g., Mitchell and Singh, 1993; Carroll et al., 1996).

With this insight in mind, I present in this dissertation a study that decouples market incumbency from organizational experience. I walk away from the current hypothesis of incompetence in research and development of a radical new technology in the case of incumbents. I instead construct a framework highlighting the competitive disadvantages (organizational inertia) and advantages (competence re-use) that apply to all established firms (incumbents and diversifying entrants) vis-à-vis de novo firms. I operationalize this study within the context of the market for anti-cancer drugs while this market transitions from cytotoxic ("random") to targeted ("mechanism-driven") drug development as a consequence of the biotechnology revolution.

I find support for the relevance of distinguishing between diversifying and de novo entrants. In fact, in statistical analyses, it is established vs. de novo firms, and not incumbents vs. entrants, that become the relevant populations to compare. Based on further results, I discuss two more propositions. First, whether R&D competences can be decomposed into a technology-specific side and an application-specific side, where the latter represents a unique source of competitive advantage for incumbents even when technologies radically change. And second, whether we should expand attention beyond the advantages of being the first to move into a market, towards being the first to move into a technological competence.

Thesis Supervisor: Thomas J. Allen

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To oncologists, cancer research scientists...  
and all human beings who make fighting for others their daily jobs.





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**My committee and me after my dissertation defense on April 28, 2006 (from left: Roberto Fernandez, Jesper Sørensen, me, Tony Sinskey, Tom Allen, and Jim Utterback).**

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## Chapter 1

# Introduction

In the present dissertation I address once more the long-standing topic of the failure of incumbent firms in a market disrupted by technological change, that is, the Schumpeterian dynamics of “creative destruction”<sup>1</sup> (Schumpeter, 1939, 1950). I do so, nevertheless, from a different starting point. I approach the review of the literature and the design of the research not initially with the intention of finding another determinant of incumbent failure, but with the intention of organizing the determinants we already have in order to find the loose ends. As I find those disconnected pieces of theory, I build a more accurate framework to guide my data collection and analysis. With this framework in mind, I am able not only to revise one of the long-standing conclusions held in creative destruction but also to explore and develop new propositions.

To accomplish this, I start in Chapter Two with a general review of the literature in management of technology that addresses the determinants of incumbent failure (and sometimes success) in a market undergoing a change in technology. I conclude that chapter with a characterization of the innovation process during the disruption as a sequence of three iterative stages: the decision to invest in the new technology, the research and development (R&D) of products

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<sup>1</sup> That is, the dynamics through which a seemingly stable market is disrupted by technological change, and moves into increasing turmoil and then back to increasing stability (Abernathy and Utterback, 1978).

under the new technology, and the commercialization of new products. I can then concentrate on one stage of the process only, making it possible to control for a more manageable list of competing hypotheses amidst the vast list of competing mechanisms documented in the literature. I choose to target the stage of the process most relevant to my interest: the R&D of products under the new technology.

I can now concentrate solely on the determinants of difference in competence in researching the new technology between incumbents and entrants, and this is my objective in Chapter Three. The central study here is Henderson (1993) who argues for incumbents' "incompetence" (i.e., lower productivity) in researching the new technology when compared to entrants. Following the "chain of causality" (Porter, 1991) common in strategy research, I ask then where those differences in research competence come from. The differences in research competence of incumbent vs. entrant firms are explained in the literature through theories about established vs. de novo firms (e.g., Nelson and Winter, 1982). These theories imply that incompetence is a consequence of organizational inertia and hence of prior organizational experience. A disconnect arises because, more often than not, the most competent and successful entrants are established (i.e., experienced) firms themselves (i.e., diversifying entrants). In fact, the argument for the liability of organizational inertia is based on theories about adaptation challenges for *any* given established firm. Consequently, the liability of inertia should apply to all established firms in competition, both incumbents and diversifying entrants. I therefore propose to decouple market incumbency from organizational experience by identifying the three populations of firms in competition: incumbents, diversifying and de novo entrants. This element of research design will then appropriately assign

the disadvantage of organizational inertia not only to incumbents but also to diversifying entrants.

Next, I review recent work that suggests the flip side of organizational experience: competence re-use. Studies that choose markets where the technological change marks the birth of the market (and hence have no incumbents by definition), find that diversifying entrants (the only established firms in their sample) outperform de novo firms (Mitchell, 1994; Carroll et al., 1996; Klepper and Simons, 2000). The advantage is traced back to the re-use of competences from prior organizational experience. I therefore propose to unpack the disruption to the R&D process into sub-categories that capture variance in levels of competence destruction to appropriately assign the advantage of competence re-use not only to diversifying entrants but also to incumbents.

With this insight in mind, I end with the construction of a framework for the analysis of R&D competence during a period of technological change: using de novo firms as a baseline, we see that established firms (both incumbents and diversifying entrants) will enjoy an advantage and a disadvantage stemming from their prior experience (namely, competence re-use and inertia, respectively). It is in the total sum that different populations of firms will fare better or worse. Although the specific prediction of performance might not be easily generalized in the current state of the literature, I certainly consider the framework generalizable.

Given that in Chapter Three I define the required elements for research design (i.e., the distinction of three populations of firms and the distinction of R&D sub-categories that vary in competence destruction), I set out in Chapter Four to find an appropriate setting for data collection along with proper data sources to

triangulate for measurement. I explain here the reasons for the setting of choice, the market for anti-cancer drugs, and document in full the firms under study, the technological disruption, the competences in R&D, and the control variables for the intended statistical analyses.

In Chapter Four I conclude that the R&D of anti-cancer drugs had three main levels of disruption caused by the biotechnology revolution: preclinical drug design as “high”; manufacturing process design as “medium”; and clinical trial execution as “low.” In Chapter Five I restrict the analysis to the comparison of preclinical and clinical competences only since they represent the two extremes in competence destruction, leaving the analysis of process design competence for Chapter Six. Through statistical analyses I find that, as expected, when both destroyed and re-usable competences are included in the analysis (i.e., preclinical and clinical), distinguishing between established (diversifying) and de novo entrants becomes relevant. In fact, the significant overarching populations of firms to compare are no longer incumbents vs. entrants, but established (i.e., incumbents and diversifying entrants) vs. de novo firms. Furthermore, I find that, counterintuitively, in an area of R&D described as entailing full competence destruction for incumbents (i.e., preclinical anti-cancer drug design), incumbent firms are leaders in performance, once more along with diversifying entrants. The least competent population of firms is de novo entrants. I propose that this result highlights the feasibility of a new proposition: whether R&D competences can be decomposed into a technology-specific side (e.g., mechanism-driven drug design) and an application-specific side (e.g., competence in the “science” of cancer as a disease). Whereas a radical change in technology would destroy the technology-specific side (i.e., technological

platforms), the application-specific side would remain for re-use. Accrued only to incumbents by the start of a disruption, the application-specific side could represent a unique source of competitive advantage for these firms.

Finally, in Chapter Six I analyze the third R&D competence category: competence in process design. The biotechnology revolution has in fact affected this area only for a sub-set of targeted anti-cancer drugs: large-molecule drugs (small-molecule drugs, although radically different in preclinical design, make use of the same manufacturing processes). In this case, although established firms outperform de novo entrants, diversifying entrants outperform incumbents. This is therefore the only R&D competence category where incumbents are outperformed. In the search for an explanation, I document the evolution of the underlying technology required for this research competence. Through interviews and quantitative historical data, I show how diversifying entrants have a first-mover advantage in the competence for large-molecule process design that later translates into a competitive advantage when they diversify into the anti-cancer drug market. I discuss then this case as something of an empirical irregularity. It moves our attention beyond first movership into a market, into first movership into a technology (i.e., a resource base) that later translates into a source of competitive advantage in a market (Lieberman and Montgomery, 1988, 1998). It also helps us think beyond the question of whether new technologies emerge applicable only to markets that tolerate lower product performance (Christensen, 1997). We move then into the larger question of adaptation to change: do incumbents have inertia in the infrastructure they use to monitor for upcoming threats (Arrow, 1974; Williams and Mitchell, 2004) and does

that inertia prevent these firms from starting adaptation attempts early enough (Hannan and Freeman, 1989)?

I end this dissertation with a discussion in Chapter Seven of the central literatures that form the background of this line of research. The key perspective is that presented by Porter (1991), which argues for attention to not only “cross-sectional” (heterogeneity in firm performance and its determinants) but also “longitudinal” (source of such heterogeneity in the determinants themselves) concerns in strategy research. As we delve deeper into heterogeneous resource bases as explanations of heterogeneous firm performance (Penrose, 1959; Wernerfelt, 1984; Rumelt, 1982, 1984; Teece, Pisano, and Shuen, 1997), we will necessarily delve deeper into evolutionary (longitudinal) dynamics (March, 1981; Nelson and Winter, 1982; Hannan and Freeman, 1984, 1989). That implies paying greater attention to the destruction of competences over time; to the decomposition of competences into their destroyed and re-usable components; and to the processes of inertia that generate a loss in efficiency as firms, seeing their competences destroyed, try to adapt to the change.

## Chapter 2

# Creative Destruction and the Determinants of Incumbents' Failure

### 2.1 The Phenomenon of Creative Destruction

Beginning with Schumpeter (1934, 1950) and motivated in part by the impact that technological change has on economic growth (Solow, 1957),<sup>2</sup> a long research tradition has studied the disruptions generated in the economy by technological change. Although the technological disruption takes place at the industry level (e.g., the automotive industry) and therefore affects the entire supply chain to different extents (e.g., automobile as well as tire producers), the firm-level analysis of strategic action has always been centered on a relevant market (either the market for automobiles [Abernathy, 1978] or the market for tires [Sull, Tedlow and Rosenbloom, 1997]) since a market is the basic focus of competition (the basic definition of a market in economic theory is a set of products that are substitutes for one another).

For example, the “electrification revolution” generated waves of disruption that sequentially impacted a diversity of markets: telegraphy in 1810, residential illumination in 1879, street cars in 1887, tabulators in 1923, typewriters in 1936 and calculators in 1937, to name a few (DuBoff, 1979, p. 4-7; Majumdar, 1982;

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<sup>2</sup> See Griliches (1996) for a historical review of the debate on the measurement of the impact of technological change on economic growth.

Utterback, 1994; Yates, 2005). Still, traditional research on strategic action has centered on the dynamics of firms within a specific market under disruption (e.g., the market for typewriters [Utterback, 1994]).

Characteristically, the market disrupted by technological change undergoes a period of transition during which both old and new technologies compete in the market. These periods can last up to twenty years or even longer depending on the market (Cooper and Schendel, 1976). It is during that transition period that firms that were present in the market prior to the disruption (*incumbent* firms) face new competition from firms that enter the market (*entrant* firms), precisely because the appearance of the new technology lowers barriers to entry. In fact, evidence shows that because the transition period can be considerable and because during those years both old and new technologies remain profitable, not only incumbents but also entrants invest in the old technology simultaneously with the new (Henderson, 1988; Snow, 2004). The old technology then experiences a boost in performance before dying (Utterback, 1994), but that boost can be traced back not just to incumbents (Snow, 2004).

Once the transition ends, the market stabilizes and enters a “regime” in which only the new technology is available (Abernathy and Utterback, 1978). It is after this transition has taken place that, retrospectively, an empirical regularity is observed: incumbent firms frequently lose their market leadership to entrant firms. In fact, the longitudinal perspective of the phenomenon describes a market that alternates between periods of stability and periods of disruption (see Figure 2.1, lower panel). It is for that reason that the question of incumbent failure was initially described as a “productivity dilemma” (Abernathy, 1978). Firms inside the market



perfect their current competences in order to outcompete their adversaries and survive (see Figure 2.1, stage 1). Yet they do so only to face a future where those competences are not only destroyed by technological change, but also represent the source of their inability to adapt to such change and hence the reason for their death in the market (see Figure 2.1, stage 2).

## **2.2 Creative Destruction and Incumbent Failure**

The empirical regularity of incumbent failure and hence of firm substitution in a market is a source of considerable socioeconomic advantages, such as the destruction of monopoly power, and disadvantages,<sup>3</sup> such as the inefficient re-absorption of incumbents' employees into the labor market or into the rest of the corporation.<sup>4</sup> Despite the importance of such implications, scholars have reached little consensus on the determinants of incumbents' lower market performance during these technological discontinuities (e.g., Tushman and Anderson, 1986; Henderson and Clark, 1990; Christensen and Bower, 1996; Tripsas and Gavetti, 2000).

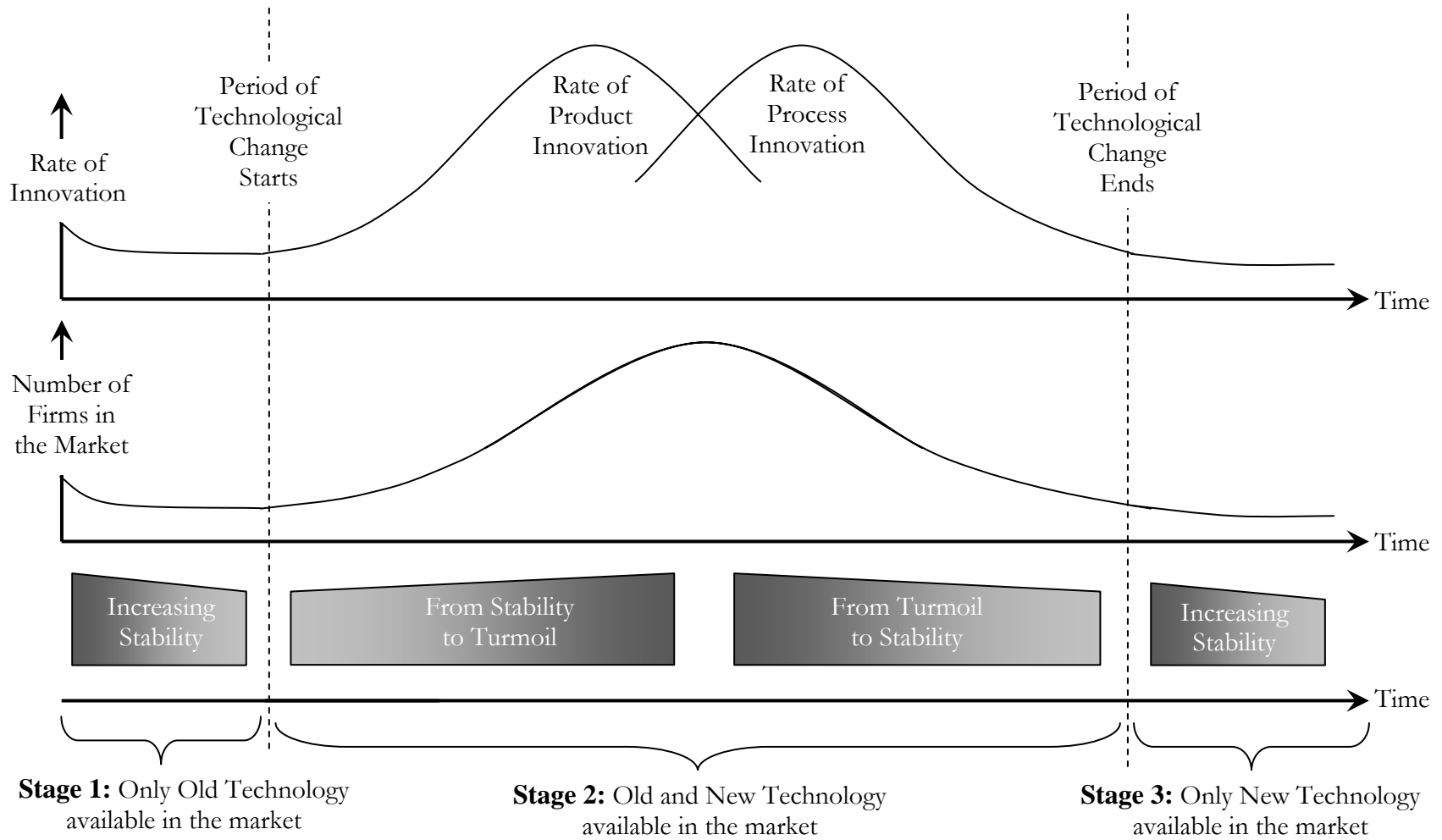
Many studies in Technology Strategy and Management of Technology have tried to parse out different determinants of market leadership (i.e., market share) and market survival (i.e., presence in the market over some minimum market share) after a period of technological change.

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<sup>3</sup> In fact, although creative destruction is widely regarded as socially desirable (i.e., advantageous) since it supports market leaders' turnover, there is little known about how the death of a firm (or subunits of it) is socially undesirable. Sociologists have, however, noted as socially costly the fact that society prefers permanent organizations vs. other forms of collective action (Hannan and Freeman, 1989, p. 72). In such discussions, at least part of that "cost" is precisely the socially undesirable losses that result if the organization is disbanded. Emerging research is now targeting the question of firm death and its consequences (e.g., Hoetker and Agarwal, 2006).

<sup>4</sup> The empirical regularity is that firms fail in a specific market. This does not imply that the firm itself dies unless this was the only market in which the firm was present.

**FIGURE 2.1**  
**The Dynamics of Creative Destruction**  
 (adapted from Utterback, 1994)



Explanatory factors for the demise of incumbents abound, including

1. Top management's (unconscious) refusal to abandon the status quo where the old technology prevails (e.g., Tripsas and Gavetti, 2000 refer to Top management's refusal to switch to a new business model);
2. Top management's refusal to "betray" the geographic region in which the firm has operated in order to adapt to the new technology (Sull, Tedlow and Rosenbloom, 1997);
3. Top management's decision to invest only (or primarily) in the technological changes that can, in the short run, provide a benefit to current main customers (Christensen and Bower, 1996);
4. Firms' incumbency status leading them to invest either too early or too late in the new technology (Cooper and Schendel, 1976; Christensen, Suarez and Utterback, 1998). Investing too early commonly leads to early disenchantment with the new technology, resulting in either early cessation of the project(s) or intermittent investment. Investing too late leads to the loss of any first-mover advantages that might exist in the industry;
5. Organizational inertia in building new firm competences, structures and operating routines (Tushman and Anderson, 1986; Henderson and Clark, 1990);
6. Battles between the groups whose status inside the firm is tied to the supremacy of the old technology, and those whose mission is to develop the new one (Morrison, 1997). Groups committed to the old technology can decide to distort or hide relevant information (such as lessons learned or technological information) from the groups working on the new technology, therefore impacting the latter's research productivity;
7. One exception is found if incumbent firms hold sole ownership of appropriate complementary assets to commercialize their inventions in the focal market (Tripsas, 1997 discusses particular instances such as lack of proprietary fonts necessary for customers to adopt the newly developed digital typesetter).

And this list contains only competing explanations that have *formally* been studied within the context of creative destruction. We still do not know, for example, whether the final market successes of incumbents and entrants whose new products differ in the five dimensions that Rogers (1962) considers central to the adoption process (relative advantage, compatibility, observability, trialability and complexity) are significantly different. Or if for end-user markets, large differences in marketing strategies and branding result in large differences in market shares for

incumbents and entrants. Add to these factors other market characteristics such as lock-in and network effects and the picture becomes increasingly complex.

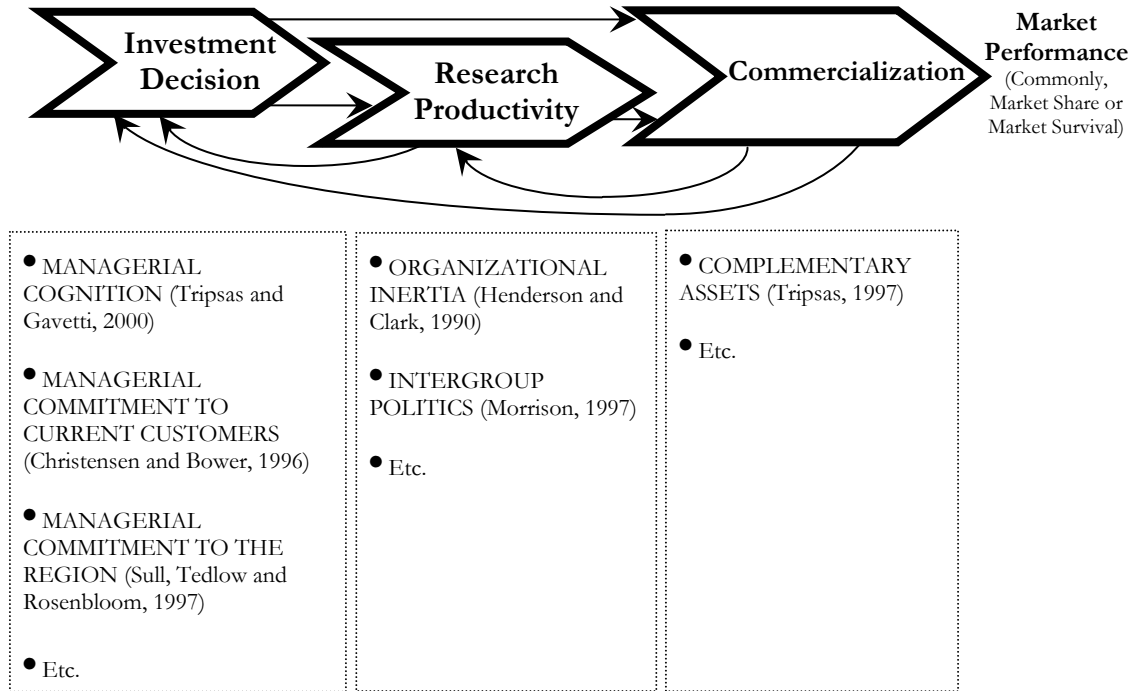
The list of competing hypotheses has grown so large that at the present no single new study can be designed to cover all alternative hypotheses with enough breadth and depth to make a significant contribution.

Therefore, my first proposition in this study is to open the black box of the innovation process and focus on narrower predictions within that process. With this objective in mind, I claim that, although the literature has concentrated on predictions of firm-level market performance, three distinguishable iterative discourses can be recognized on the mechanisms argued to give rise to such predictions: investment decisions, research productivity (i.e., the R&D process) and commercialization strategy. Such discourses and examples of the most representative research in each of them are depicted in Figure 2.2 (next page), and their classification is explained next.

To understand the construction of Figure 2.2, a look back at the list of main explanatory factors presented above is necessary. In that list, the first 4 items are differences in investment decisions, such as top management refusing to invest in the new technology because it will not benefit current customers in the short run. Investment decisions include whether to invest in the new technology, but also how much and how early to invest, when to stop funding the project (e.g., fund the early research but not the late development of the new technology [Cooper and Schendel, 1976]), or suboptimal choices for investment (e.g., to invest in retooling an existing facility instead of more cheaply building a new one in another region [Sull et al.,

1997], or to make funding contingent on particular specifications for the commercialization strategy [Tripsas and Gavetti, 2000]).

**FIGURE 2.2**  
**Different Discourses in the Creative Destruction Literature**  
**to Explain Incumbent Failure**



Those differences in investment will then impact the productivity of the R&D process (through their effect on resources allocated or specifications required) and/or the success of the commercialization process (through their effect on resources allocated or commercialization strategy required). In some cases, investment decisions can even result in some firms being forced to exit the market. In the case of the R&D process, differences in investment will join mechanisms 5 and 6 to determine differences in R&D productivity (also termed research

productivity or research competence). The fact that a firm starts investing later than its competitors in the research of the new technology will, for example, add to the internal political battles between the research teams in charge of the old technological projects and those in charge of the new ones (battles that result in purposeful sabotage, for example) to exacerbate the firm's resulting low research productivity. It is because of this that prior research suggested measuring separately "underinvestment" and research "incompetence" in order to understand incumbents' market failure (Henderson, 1993).

Finally, differences in R&D productivity will join differences in resource allocation or commercialization requirements stemming from former investment decisions, as well as mechanism 7 to determine differences in final market share.

Notice that the claim is not that firms do not iterate through their project execution (i.e., the claim is not that firms make a decision to invest and execute it without changes over time). The claim is rather that, per time unit (in most cases one year or quarter as a budgetary period) firms decide to invest, run R&D functions and commercialization attempts, evaluate their actions, and use the feedback gathered to act on the next time unit.

Once the literature is seen in the light of these three discourses, narrower tests can be designed to explain heterogeneous managerial investment separately from research productivity and separately from commercialization strategy during periods of technological change. Furthermore, narrower questions can then make use of outside literature to inform specific hypothesis (e.g., research in consumer behavior can inform differences in commercialization strategies between incumbents and entrants). Conclusions from such narrower tests can then be pulled together to

understand in better detail the determinants of market performance during periods of technological change.

Therefore, I start this study by opening the black box of the innovation process in the literature on creative destruction with the objective of sacrificing breadth for depth. I now focus on a specific part of the innovation process during a period of technological change: the R&D process. Chapter Three then concentrates on a narrower issue: differences in competence in researching the new technology between incumbents and entrants.

## Chapter 3

# Differences in Competence to Research the New Technology

Amidst the debate within the creative destruction literature on the determinants of incumbents' market failure, scholars do agree that within research-intensive industries, one of the most significant determinants, after controlling for underinvestment, is these firms' "incompetence" in researching the new technology (Henderson, 1993). Such differences in the research competence of incumbent vs. entrant firms are explained in the literature through theories about established vs. de novo firms (e.g., March and Simon, 1958; Galbraith, 1973;<sup>5</sup> Arrow, 1974; Nelson and Winter, 1982). A disconnect arises because, more often than not, the most competent and successful entrants are established firms themselves (diversifying entrants).

### 3.1 Incumbency, Structural Inertia and Organizational Change

In their landmark study in the creative destruction literature, Henderson and Clark (1990) offered in-depth qualitative evidence of four waves of architectural innovation in the market for photolithographic alignment equipment. As the

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<sup>5</sup> The dynamics in Galbraith (1973) relate to issues of increasing organizational size and not of experience per se. This work explains how as organizations accrue experience they *also* grow in number of employees and encounter a dilemma of differentiation vs. integration (Lawrence and Lorsch, 1967). It is in the attempt to resolve such dilemmas that organizations engage in departmentalization and general organizational design (Galbraith, 1973).



authors explained, in each wave of disruption incumbents consistently underperformed entrants in the research and development of the new technology. A representative example of the dynamics of incumbents' research incompetence is Kasper Instruments' failure in the face of Canon's entry into this market. When Canon, the entrant firm, introduced its innovative proximity aligner in 1973, Kasper Instruments, the incumbent, asked its own engineers to evaluate the competitor's piece of equipment. The team of engineers "overlooked" the new features in Canon's proximity aligner because they were "blinded" to them by the inertia of their former organizational experience. That is, organizational inertia leads to incumbents' incompetence at innovation.

In later work, Henderson (1993) explained that incumbents can be found to underinvest if the innovation is radical in the economic sense, and/or to be incompetent in research if the innovation is radical in the organizational sense, and that the two conditions are orthogonal and should be distinctively measured. The author explained that an innovation is radical in the economic sense if the monopoly price under the new technology is below the cost of producing under the old technology, following Arrow (1962). In contrast, an innovation is radical in the organizational sense when it challenges the organizational status quo. It is in this latter case that the organization exhibits inertia, a resistance to organizational change aiming at the perpetuation of the status quo. In cases where the innovation is radical in the organizational sense, inertia would diminish incumbents' ability to innovate and would explain their research incompetence in the new technology.

Although Henderson and Clark (1990) had previously explained that innovations in the photolithographic alignment equipment market were architectural

in terms of the product, Henderson's (1993) later analysis applies to the general phenomenon of innovations that have an impact that is "radical in the organizational sense" on incumbent firms. Therefore, Henderson's (1993) conclusion applies to all "non-incremental" (i.e., radical, architectural and modular) innovations.

During the years prior to each disruption, Henderson (1993) explained, incumbents must have built a specific organizational structure, a set of communication channels and information filters (March and Simon, 1958; Galbraith, 1973; Arrow, 1974) to become efficient in the research and development of their current-generation aligners. This efficiency then marked the firms' market demise when a significant change in the organizational structure became necessary in order to develop the next-generation aligner. In the face of technological change that posed a challenge that poses radical in the organizational sense, incumbents' attempts to use available resources for a new endeavor became a larger disadvantage than starting from scratch. Organizational inertia leads to research incompetence.

However, if organizational inertia is present among incumbents only and explains their incompetence (and later market underperformance), then competent entrants must be a homogeneous category of firms without organizational-level inertia. That is, competent entrants must be a homogeneous category of firms for which the new products in this market do not represent an organizational change, do not represent a transition from current to new products. That implies that competent entrants are a homogeneous category of de novo firms. This, however, contradicts empirical evidence. More often than not, the most competent and successful entrants are established firms themselves (diversifying entrants).

In Table 3.1, I take classic work in creative destruction and separate entrants into diversifying (i.e., experienced/established)<sup>6</sup> vs. de novo entrants. Data clearly show that there is a significant presence of diversifying firms among entrants.

**TABLE 3.1**  
**Significant Presence of Diversifying Firms among Entrants**  
**in the Creative Destruction Literature**

Study	Industry / Radical Innovation	Entrants	
		Diversifying	De Novo
Tripsas, 1996, 1997	Analog Phototypesetters	94%	6%
	Digital CRT Phototypesetters	86%	14%
	Laser Imagesetters	100%	0
	Laser Postscript Imagesetters	57%	43%
Tushman and Anderson, 1986	Cement	13 / 19	6 / 19
	Commercial Airlines	12 / 12	0 / 12
	Minicomputers	17 / 21	4 / 21
Cooper and Schendel, 1976, seven industries including: <ul style="list-style-type: none"> <li>• steam locomotives vs. diesel-electric</li> <li>• fountain pens vs. ball-point pens</li> <li>• leather vs. polyvinyl chloride and poromeric plastics</li> </ul>		Most entrants were established firms	
Peck, 1961	Aluminum	6 / 7	1 / 7
Enos, 1962	Petroleum extraction	7 / 7	0

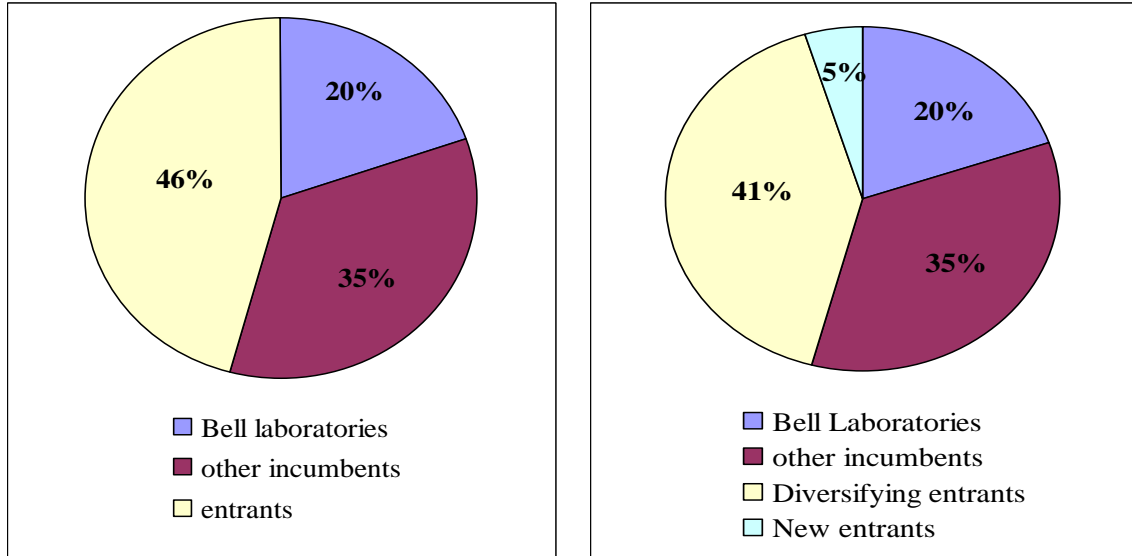
Next, in Figure 3.1, I analyze again Tilton’s (1971) account of the transistor revolution 1952-1968 (i.e., the transition from receiving tubes to transistors) to offer evidence that diversifying entrants are not only significantly present among entrants, but are also some of the most active innovators among these firms. Tilton (1971) reports (Table 4-2 in the original) the patenting activity per firm of all firms in this market during the transition. Although the author classified firms in the classic incumbent and entrant categories, I traced the corporate history of each entrant firm in historical sources such as the *Moody’s Industrial Manual* collection. I found that

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<sup>6</sup> I use the words “experienced” and “established” as interchangeable terms. My intention is to use organizational experience (a concept I will define in detail in section 3.3) as a binary variable that firms either had (experienced/established) or did not have (de novo) prior to starting research on the new technology.

approximately 89% of all patents generated by entrants (corresponding to 41% overall) in that period came from diversifying entrants.

**FIGURE 3.1**  
**Proportion of Total Patents by Firm Category,**  
**during the Transistor Revolution**



Source: Adapted from Tilton (1971).

Notes:

(1) Because of Bell Laboratories' strong role in the invention and evolution of the transistor, this firm, though an incumbent, is usually tracked separately in analysis of innovative effort.

(2) Though Tilton (1971) tracks the Transistor Revolution from 1952 to 1968, the patenting in this graph represents 1961, a mid-range point, chosen as representative.

Finally, in Table 3.2 I perform the same additional analysis of Tilton's (1971) account of the transistor revolution, but this time in terms of yearly market share (Table 4-5 in the original). I find as well that 2 out of the 3 top sellers in those years were diversifying entrants, showing that this category of firms is not only significantly present among entrants and represents some of the most innovative entrants, but that it also represents some of the most successful market successors.

**TABLE 3.2**  
**Diversifying Entrants among Leading Firms in terms of Market Share,**  
**during the Transistor Revolution**

Company Name in 1952*	Founding Date (and Name at Founding)	Original Class in the Cited Source	Further Classification of Entrants	US Semiconductor Market Share (%)	
				1957**	1966**
Bell Laboratories (Western electric)	--	Incumbent	Incumbent	5	9
General Electric	--	Incumbent	Incumbent	9	8
RCA	--	Incumbent	Incumbent	6	7
Raytheon	--	Incumbent	Incumbent	5	b
Sylvania	--	Incumbent	Incumbent	4	b
Philco-Ford	--	Incumbent	Incumbent	3	3
Westinghouse	--	Incumbent	Incumbent	2	5
Others (receiving tubes)	--	Incumbent	Incumbent	2	3
Texas Instruments	1930 (Geophysical Service Inc.)	Entrant	Diversifying entrant	20	17
Transitron	1952	Entrant	De Novo entrant	12	3
Hughes	1932 (Aircraft Division within the Hughes Tool Company)	Entrant	Diversifying entrant	11	b
Motorola	1928 (Galvin Manufacturing Corp.)	Entrant	Diversifying entrant	b	12
Fairchild	1957	Entrant	De Novo entrant	b	13
Thompson Ramo Wooldridge	Around 1928	Entrant	Diversifying entrant	b	b
General Instrument	1923 (General Instrument)	Entrant	Diversifying entrant	b	4
Others (entrants)		Entrant	unclassified	21	16
			TOTAL	100	100

Source: adapted from Tilton (1971).

\* Year of start of the Transistor Revolution.

\*\* Top 3 firms in terms of market share of the respective year are shaded.

Notes: (1) Tilton (1971) tracks the Transistor Revolution from 1952 to 1968. Two mid-range points, years 1957 and 1966, are selected as representative here. (2) "--" means irrelevant for the argument in question.

Figure 3.2 presents a diagram of the implication of this disconnect between theory and evidence.

**FIGURE 3.2**  
**A Disconnect in the Creative Destruction Literature**  
**when Market Incumbency and Organizational Experience are confounded**

(3.2a). Common design in studies of creative destruction

<i>Market Incumbency</i>	
Market Incumbents	Market Entrants
<b>Low</b> Research Competence	<b>High</b> Research Competence

(3.2b). Differences in the competence to research the new technology among firm categories, as seen when decoupling market incumbency from organizational experience

		<i>Market Incumbency</i>	
		Market Incumbents	Market Entrants
<i>Organizational Experience</i>	Established Firms	<b>Low</b> Research Competence <i>(incumbent)</i>	<b>High</b> Research Competence <i>(entrant)</i>
	De Novo Firms	X	X

(3.2c). Mechanisms behind the differences in the competence to research the new technology among firm categories, as seen when decoupling market incumbency from organizational experience

		<i>Market Incumbency</i>	
		Market Incumbents	Market Entrants
<i>Organizational Experience</i>	Established Firms	<b><i>Incumbents</i></b> <ul style="list-style-type: none"> <li>• Inertia from Old Routines</li> <li>• Inertia from Old Structure</li> <li>• Etc.</li> </ul>	X
	De Novo Firms	X	<b><i>Entrants</i></b> <ul style="list-style-type: none"> <li>• No Inertia from Old Routines</li> <li>• No Inertia from Old Structure</li> <li>• Etc.</li> </ul>

Panel 3.2a shows the prediction in research competence: incumbents underperform entrants in researching the new technology. Then panel 3.2b “decouples” market incumbency from organizational experience as two orthogonal axes and shows how the data is collected and analyzed: incumbents are compared to all entrants aggregated, including those entrants that are established firms and those that are de novo ones. Finally, panel 3.2c shows how the argument that prior organizational experience leads to organizational inertia (i.e., to a resistance to change) evolves. It is in the discrepancy between panels 3.2b and 3.2c that the theoretical disconnect arises.

In fact, studies outside of creative destruction provide evidence that, like incumbents, diversifying entrants exhibit the disadvantage of organizational inertia resulting from their prior organizational experience.

In a study comprising 35 years of history of the diagnostic equipment industry, Mitchell and Singh (1993) examined a set of established firms as they decide to diversify into new markets whose birth is the result of specific technological innovations.<sup>7</sup> Although the firms are *industry* incumbents, they are not *market* incumbents as commonly analyzed in the creative destruction literature. In fact, they represent diversifying entrants into such newly born markets, markets that exhibit no market incumbents by definition (since the markets are just born, there are no predecessors, market incumbents from the prior technological regime). The authors explained that diversifying firms are subject to “... inertia induced by bureaucracy [Cozier, 1964]...” (p. 152), an argument similar to that previously discussed for incumbents.

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<sup>7</sup> For example, as Nuclear Magnetic Resonance was invented, the market for Magnetic Resonance Imaging (MRI) equipment was born.

Indeed, in a well-known study that combines research in corporate diversification and in new product development, Leonard-Barton (1992) examines in detail the intersection between corporation and project. The author studies a sample of ten projects where two projects were chosen from each of five firms as extremes on a scale of degree of alignment with each firm's core capabilities. The author concludes that the core capabilities of these firms became their core rigidities when significant innovation was necessary. The author was not interested in the intersection between corporation and market and therefore did not distinguish whether each project was targeting a market where the firm already had a presence (i.e., market incumbency) or a market where the firm intended to diversify (i.e., market entry/diversification).<sup>8</sup> But based on her careful description of selected projects one can see that some projects are attempts of a market incumbent to innovate (e.g., the Ford Motor company generating a new compressor for an air conditioner system), and some are attempts of a firm to incur diversification into other markets (e.g., an anonymous chemicals firm investing in the "factory of the future"). Irrespective of market incumbency, all projects are indistinguishably difficult to pursue when they are misaligned with the core capabilities of the firm. The organizational processes that gave rise to these firms' rigidities are traced back to broad-range theories about established firms in general: the emergence of core capabilities (Teece, Pisano and Shuen, 1990); of status differentials among groups inside the firm (Burns and Stalker, 1966); of a distinctive organizational culture (Shein, 1984); and of a set of organizational values that reflect the imprinting of

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<sup>8</sup> The author specifically clarifies: "... [projects under study] were neither incremental enhancements nor small undertakings. Nor did incongruent projects necessarily involve 'radical' innovations by market or technological measures... Rather, unaligned projects were nontraditional for the organization along several dimensions of the selected core capability" (Leonard-Barton, 1992, p. 258).



company founders (Kimberly, 1987). The study implies that all established firms generated core rigidities that led to inertia. The extent of such inertia, however, was related to the extent of misalignment between organization and project, not to incumbency or entry (i.e., diversification) status.

Finally, Chesbrough and Rosenbloom (2002) also present a diversifying entrant subject to organizational inertia. In a study of Xerox Corporation, the authors show how the established firm failed to successfully capitalize on a diversification attempt because it insisted on holding on to the business model of the past.

Indeed, around the same time in which Henderson (1988, 1993) and Henderson and Clark (1990) originally proposed to further our understanding of the economic phenomenon of incumbent failure through theories of structural inertia and organizational change (see discussions in the original on March and Simon, 1958; Cyert and March, 1963; Burns and Stalker, 1966; Galbraith, 1973; Arrow, 1974; Nelson and Winter, 1982), Hannan and Freeman (1989) published their treatise arguing that theories of structural inertia and organizational change were themselves incomplete. Theories of structural inertia and organizational change, as Hannan and Freeman (1989) pointed out, have the organization as the unit of analysis. They are what the authors previously described as theories focused on “a single organization facing an environment” (Hannan and Freeman, 1977, p. 933). In order to apply these single-organization theories to the study of competition among categories of firms during a period of technological change, identifying the scope conditions of the

theories becomes the key cornerstone.<sup>9</sup> This is precisely my proposition in this study: the scope condition of these theories is not market incumbency but organizational experience. To recognize this difference, the two constructs need to be decoupled. Since theories of inertia and change are theories about each single established (i.e., experienced) firm and its environment, they should apply, even if to different degrees, to all established (incumbents and diversifying) firms in competition.<sup>10</sup>

The application of single-organization theories of inertia to the explanation of replacement of the incumbent firm category requires then additional nuancing. Although there might be variance in the level of inertia present in incumbents vs. diversifying entrants, there will be variance among incumbents and among diversifying entrants as well. Whether the between-category variance is larger than the within-category variance is an open question. This is precisely the idea posed originally by Hannan and Freeman (1977) when first discussing adaptation vs. replacement:

“Since all organizations are distinctive, no two are affected identically by any given exogenous shock. Nevertheless, we can identify classes

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<sup>9</sup> Indeed, a key question in theories of structural inertia and organizational change, Hannan and Freeman (1989) explain, is a rarely attended-to change in the unit of analysis. Theories of change emphasize adaptation and hence focus on the organization facing its environment. In contrast, change in the absence of adaptation would occur by replacement and take place at the level of the population of organizations, the next level up in units of analysis. A crucial element of the theoretical disconnect outlined in this chapter lies precisely in the change in the unit of analysis from firm to firm category, and more explicitly, in the relevant category for implementation.

<sup>10</sup> To observe this, notice that every established firm builds communication channels and information filters to increase their efficiency (Galbraith, 1973; March and Simon, 1958; Arrow, 1974); develops routines to better perform the tasks at hand (Nelson and Winter, 1982); and gives rise to internal groups whose power and status become ingrained in the status quo (Burns and Stalker, 1966). When faced with the challenge of organizational change, these same routines, communication channels, information filters, and power and status structures give rise to the organizational inertia that inhibits the organization’s ability to adapt to the change (in the case of innovations that are radical in the organizational sense, organizational inertia inhibits the ability to innovate).

of organizations which are relatively homogenous in terms of environmental vulnerability” (p. 934).

A particular reason is necessary to hypothesize that incumbents will have stronger inertia than diversifying entrants as a category of firms. Otherwise, the only prediction available is that established firms, whether incumbents or diversifying entrants, constitute an overall firm category prone to some degree of inertia (that they might compensate for) while de novo firms will not have (firm-level) inertia by definition.

### **3.2 Established Firms and Corporate Diversification**

Some evidence can be gathered regarding the comparison of incumbents and diversifying entrants as sub-categories of established firms in terms of their approach to organizational change. Specifically, studies in corporate diversification have looked at all established firms without distinguishing those marked by market incumbency, and hence they provide a good source of possible evidence to borrow.

The first point to explore is whether the technological change represents cannibalization only for incumbents and hence, it becomes obvious that it is rational only for incumbents and for the individuals within them to resist change. The most commonly cited source for the argument of resistance to innovation by incumbents is Arrow (1962). Yet, in the original model the author stated that in the monopolistic situation, only the monopolist itself could invent. “A situation of temporary monopoly... which does not prevent the entrance of new firms with innovations of their own, is to be regarded as more nearly competitive than monopolistic” (Arrow, 1962 p. 619). Therefore, by the author’s own logic, resisting the new technology in

the name of resisting cannibalization is *not* an option when barriers to entry have been lost, which is always the case for technological change that induces diversification from other markets. Indeed, the most rational thing to do in such instances might be to invest in the new technology right away. In fact, it is precisely this distinction between cannibalization under blockaded vs. free entry that drives results in later models. Conner (1988), for example, concluded that incumbents would invest immediately in the new technology, then shelve the invention, and wait to launch it until an entrant launches its own product in the market. The incumbent's lag between investment and launch is precisely to avoid cannibalization. But launching immediately after (in fact, simultaneously with) the entrant is rational since once there is entry, the loss of the old technology's revenue is concomitant. That is, once the entrant launches, the incumbent does not have a choice: either it challenges its own revenue (i.e., cannibalizes), or the entrant will.

Furthermore, recent research in corporate diversification calls attention to the distinction between intra-temporal vs. inter-temporal economies of scope (Helfat and Eisenhardt, 2004). Although intra-temporal economies of scope correspond to the standard scenario where a firm diversifies its cross-sectional scope, inter-temporal economies of scope correspond to cannibalization dynamics. That is, the definition of diversification under inter-temporal economies of scope refers precisely to the process of expansion where firms diversify in order to exit their current markets.<sup>11</sup>

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<sup>11</sup> Beyond the case study presented in Helfat and Eisenhardt (2004), Burgelman's (1994) account of Intel's move from memory products into microprocessors corresponds to the same dynamics.

In other words, for both sets of established firms, the change in technologies (for incumbents) or markets (for diversifying entrants) might carry a certain degree of cannibalization.

A second point to consider in the search for differences between incumbents and diversifying entrants as established firms facing change is whether the dynamics represent a threat to the firm survival only for incumbents. After all, diversifying entrants attempt expansion but keep their base business intact whereas incumbents' base business is under disruption. Yet in fact, in the previously mentioned study by Mitchell and Singh (1993) of the medical diagnostic industry, the authors discuss how the dynamics of diversification may disrupt successful routines in the base business as well. They find that diversifying entrants that successfully expand enjoy an additional premium in their performance in their base business. But those with failed expansion attempts experience an erosion of their base business as well.

In other words, for both sets of established firms, the change in technologies (for incumbents) or markets (for diversifying entrants) has an impact on their base business.

Finally, a third point to consider in comparing incumbents and diversifying entrants as they face organizational change is whether only the latter can in fact make a decision on whether to invest. Incumbents might seem to be stuck in the market under disruption. In fact, a classic framework within the same corporate diversification literature considered market incumbents facing a leap from an old to a new technology as a special case of the larger diversification scheme. Roberts and Berry (1985) explained how the choice a firm makes to incur diversification can be represented by a "map" where the vertical axis is a radical change in technologies and

the horizontal axis is a radical change in markets. The firm confronts the decision to diversify, and different strategies (e.g., joint ventures, acquisitions) seem to be a better fit depending on what the move within this map represents for the firm. In that framework, market incumbents in the face of radical technological change are a straight vertical move on the y-axis, a special case of corporate diversification. Furthermore, when established firms undergo a diversification between technologies for a market or between markets for a technology, the options to consider are almost identical.<sup>12</sup>

In fact, recent research (Guedj and Scharfstein, 2004) has argued that the question of whether a firm can choose to continue or halt investment in a project or projects related to any technology or market is a function of the size of the firm's project portfolio. In other words, having the choice to halt the project is a function of having alternative options to fall back on and not of incumbency status.

### **3.3 Definitions: Market Incumbency, Organizational Experience, and the Firm Categories in Competition**

To continue with the present study, I next delineate key definitions.

I use *organizational experience* to refer to all processes described in the literature by which a firm gains efficiency and expertise at its current "business." Such processes therefore, help the firm become reproducible and outlive its competition. Organizational experience is intended to include all kinds of processes taking place as a firm is in operation for a particular business. It includes then processes of emerging routines (Nelson and Winter, 1982) and organizational structure (March

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<sup>12</sup> The only difference is that licensing becomes an additional viable option for market incumbents moving from an old to a new technology.

and Simon, 1958; Galbraith, 1973), but also processes of emerging power and status hierarchies within the organization (Burns and Stalker, 1966).

It is not until the firm is faced with the need to innovate in order to succeed in a new “venture” (whether across technologies for incumbents or across markets for diversifying entrants) that its organizational experience gives rise to *organizational inertia*, a resistance to change. In fact, organizational inertia is not always a disadvantage. In periods of increasing stability, an organization survives by making its operation reproducible and stable. During such periods organizational inertia is beneficial since it makes the organization reproducible and saves it from *random* change (Hannan and Freeman, 1984).<sup>13</sup> Only later does the disadvantage arise: “the very factors that make a system reproducible make it resistant to [*strategically planned*] change” (Hannan and Freeman, 1989, p. 75). That is what has been termed paradoxical by other authors (e.g., Lieberman and Montgomery, 1988) about Hannan and Freeman’s (1984, 1989) discussion of inertia being beneficial or detrimental at different times in the evolution of an organization’s relationship with its environment. The same organizational inertia that saves the firm from random change precludes it from strategically planned change. It is then that organizational inertia is a by-product of reproducibility, that is, of having been in operation, fighting to outlive competition and accruing experience as an organization. In that sense, all established firms, not just incumbents, are at risk of a “productivity dilemma” (Abernathy, 1978). As some of the entrants to a disrupted market have, like

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<sup>13</sup> This view is developed by the authors in contrast to a perspective within Organizational Theory they term “random transformation theory” (Hannan and Freeman, 1984, p. 150). Based on March’s (1981) perspective in which organizations are continually changing and this change cannot be arbitrarily controlled, Hannan and Freeman (1984) cite as random transformation theory work such as March and Olsen (1976), March (1982) and Weick (1976).

incumbents, accrued organizational experience, they should then, like incumbents, be prone to the disadvantage of organizational inertia.

It becomes important to differentiate organizational experience from its resulting disadvantage, organizational inertia, because organizational experience can provide advantages as well, as will be discussed later.<sup>14</sup>

I use *market incumbency* to refer to the presence of a firm in the focal market at the time this market is disrupted by a technological change. By definition, when a firm is a market incumbent, the firm is an experienced organization, an established firm, since the firm must have accumulated experience in at least one market (the focal market) prior to the start of the disruption under study.

Decoupling market incumbency from organizational experience allows us to see that the first is a characteristic that refers to a firm's position in a market, whereas the latter is a characteristic ascribed to the firm itself (once a firm is organizationally experienced, it carries the consequences of its experience, including some level of inertia, to every market it attempts).

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<sup>14</sup> In fact, differentiating experience from its resulting inertia, in my opinion, is important for theoretical reasons. The differentiation would then mirror the contrast between “inertia” and “momentum” in Newtonian Mechanics. Inertia in Mechanics is used to refer to Newton's First Law under which “a body left undisturbed maintains a constant velocity” (Busza, Cartwright, and Guth, 2002, p. 58; notice “constant” refers to magnitude, including zero, and/or direction). Newton's Second Law then quantifies the force necessary to disturb that body and alter its velocity as the product of mass and acceleration (where acceleration is the rate of change of velocity). Over the years following Newton's original *Principia*, scientists separated the term inertia from what is now termed “momentum” (Gondhalekar, 2001; Maltese, 2003). Momentum is defined as the product of mass and velocity, and hence, as a body accelerates, the rate of change of the body's momentum equals the force (in each instant) necessary to keep disturbing its inertia. Notice that the term inertia is used to refer to the principle only, whereas momentum is used to refer to the quantification (quantity and direction). Hence we talk about the rate of change of momentum, but not the rate of change of inertia. My intention was to achieve an equivalent separation between the organization's experience (which should be quantifiable through some proxy, both in magnitude and “direction” since it is market- and resource base-specific) and its inertia (the basic principle stating that, *ceteris paribus*, an experienced organization will resist change).



As a result of failing to decouple market incumbency from organizational experience, studies of creative destruction have systematically confounded the definitions of new (de novo) with that of new to a market (entrant), and the definitions of established (experienced) with that of established in a market (incumbent). The implementation of this decoupling requires the clear definition of three specific firm profiles. These profiles appear in Figure 3.3. Studies in creative destruction have compared incumbents vs. entrants, implying that “incumbent” and “established” are interchangeable terms (see panel 3.3a). Decoupling market incumbency from organizational experience allows us to see that the two terms are not interchangeable. Firms can be incumbents or entrants, and established or de novo firms, and the values are orthogonal (see panel 3.3b). The proper implementation of incumbency and experience as separate constructs would require all combinations possible of their two values (considering both constructs can be crudely measured as binary variables: incumbents vs. entrants and established vs. de novo). That would result in four sub-categories of firms. But the lower left quadrant is empty by definition (see panel 3.3b): an incumbent cannot be a de novo firm at the time of facing the disruption since it must have been in operation in the focal market under the old technology. That leaves the implementation of decoupling market incumbency from organizational experience as a set of three categories of firms, which are defined next.

**FIGURE 3.3**  
**Contrast of Research Designs:**  
**The Creative Destruction Literature and this Study**

(3.3a). Common design in studies of creative destruction

<i>Market Incumbency</i>	
Market Incumbents	Market Entrants
<b>Low</b> Research Competence	<b>High</b> Research Competence

(3.3b). Decoupling market incumbency from organizational experience

		<i>Market Incumbency</i>	
		Market Incumbents	Market Entrants
<i>Organizational Experience</i>	Established Firms	? Research Competence <i>(incumbent)</i>	? Research Competence <i>(diversifying entrant)</i>
	De Novo Firms	X	? Research Competence <i>(de novo entrant)</i>

*Incumbent* firms are experienced firms established in one or more markets, including the focal market at the moment this market is disrupted by the technological change. That is, they exhibit both market incumbency and organizational experience.

*Entrants* are firms that were not in the focal market prior to the period of technological change and that enter it during the transition to the new technology

(precisely because the emergence of the new technology lowered barriers to entry into this market).

*Diversifying entrants* are those entrants that were established in other market(s) prior to the start of the disruption in the focal market and that hence enter it by diversification. They therefore have prior organizational experience with the advantages and disadvantages this implies.

*De novo entrants* are those entrants born in the focal market during the period of transition between technologies and therefore have no prior organizational experience.

Clearly, *incumbents* and *diversifying* entrants are both *established* firms, that is, firms experienced in one or more markets prior to the period of technological change, regardless of whether that market(s) includes the focal market.

Intel's detailed history of movements across technologies and markets as reported in Burgelman (1994) allows me to illustrate an example of the difference between market incumbency and organizational experience. Created in 1968 to commercialize DRAM memories and replace "magnetic cores as the standard technology used" (p. 32), the company was then a *de novo* entrant into the memory products market. The company stayed in that market "for four successive product generations" (p. 35) through which it remained a market incumbent. While still in the market for memory products, engineers at Intel invented microprocessors in response to customer firm Busicom's request. As Intel gradually started its R&D and manufacturing of microprocessors during the early 1980s, it was a *diversifying* entrant into the microprocessors market, although it remained a market incumbent in the market for memory products until its exit in 1985. Observe that Intel was a

market incumbent or diversifying entrant in different markets. However, after its entry into the memory products market, its first entry into any market (hence the only time when the firm qualifies as a de novo firm), it continuously accumulated organizational experience for the rest of its corporate history. That is, in both the market for microprocessors and the subsequent product generations in the market for memory products, Intel was an established firm in competition.

### **3.4 The Flip Side of Organizational Experience: Competence Re-Use**

Decoupling market incumbency from organizational experience calls attention away from incumbency and into the dynamics of organizational experience itself.

In fact, a set of recent strategy studies examines diversifying entrants and de novo firms in competition in settings in which the technological innovation marks the birth of the market (settings that therefore include no incumbents).<sup>15</sup> In these studies, however, prior organizational experience gives diversifying entrants an advantage: the ability to re-use their previously acquired competences.

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<sup>15</sup> There are, though, studies outside of creative destruction that investigate the behavior of firms during a technological disruption that does not coincide with the birth of the market and that will therefore have incumbent firms present. However, uninterested in incumbents' dynamics, these studies do not sample them. An example is Holbrook et al., (2000) where the authors present a rich historical account of four firms competing during the transistor revolution: Sprague Electric, Motorola, Shockley Semiconductor Laboratories and Fairchild Semiconductor. My further inquiry into the corporate histories of these firms reveals they are all diversifying and de novo entrants to the market that transitioned from receiving tubes to transistors. Tilton (1971) defines the transistor revolution as starting in 1952. Based on information from Tilton (1971), corporate histories available through the *Moody's Industrial Manuals* collection and existing firms' corporate websites, I distinguished each firm's profile. Fairchild, born in this market in 1957, is a de novo entrant. Motorola was founded in 1928 as Galvin Manufacturing Corp. Sprague Electric was founded in 1926 and first appeared in *Moody's Industrial Manuals* in 1945 as selling capacitors, resistors and ceramic-coated copper wire. Shockley Transistors Corp. was created by Beckman Instruments as a wholly owned subsidiary in 1958. Beckman Instruments itself was founded in 1934 as National Technical Laboratories. These latter three firms were never present in the market for receiving tubes but were certainly in operation in other markets prior to their incursion into transistors and were therefore diversifying entrants. Because the study is not in the creative destruction literature, by design the authors did not sample incumbent firms (e.g., General Electric, Raytheon, Western Electric).

Mitchell (1994), for example, finds that diversifying entrants outperform de novo firms as measured by divestiture and dissolution rates in a study of the birth of each of seven new markets within the diagnostic equipment industry. In another study comprising a series of markets within the telecommunications and medical sectors, Methe, Swaminathan and Mitchell (1996) find diversifying entrants<sup>16</sup> outperforming de novo firms in the number of innovations introduced in each market. These authors further distinguish between diversifying entrants that come from other markets within the industry (*industry* incumbents) and those that come from outside the industry, and find the latter additionally advantaged. Even more importantly, scholars interested in differences in firm survival find that diversifying entrants (*de alio* firms) outlive de novo firms, and assert that this advantage stems from the former's ability to re-use previously acquired competences (Carroll et al., 1996; Klepper and Simons, 2000; Khessina and Carroll, 2002).

This mechanism, competence re-use, completes then the picture of established vs. de novo firms in competition. Over time, established firms build competences and underlying resource bases to support their reproducibility and survival. These resource bases might generate a disadvantage, namely inertia, when later facing change, but can generate an advantage as well, namely re-use.

Competence re-use is an advantage available only to established firms, that is, to firms that have been in operation before facing the challenge of using the new technology (a challenge to incumbents) to develop products for the focal market (a

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<sup>16</sup> In Methe et al., (1996), it is impossible to discern which of these industry incumbents are market incumbents as well (and which are just diversifying entrants) based on the information in the paper. The list of innovations presented in Table 1 (p. 1189) is described by the authors as newly born markets and should therefore have no market incumbents by definition. For Table 2 (p. 1190), however, the authors only offer details about experienced firms at the industry level. Unable to identify if there are market incumbents in the sample of Table 2, I refer to them as diversifying entrants in general.

challenge to diversifying entrants). De novo firms have nothing to re-use at the organizational level. In fact, the development of such competences, such resource bases, to support a firm's reliable operation in competition forms the basis of the understanding of heterogeneity in firm performance in the resource-based view of the firm (Penrose, 1959; Wernerfelt, 1984; Rumelt, 1982, 1984, 1991; Teece, Pisano, and Shuen, 1997). It also explains much of the reason for diversification in the first place. Research has shown that established firms tend to diversify into businesses where they re-use their resource bases (Montgomery and Hariharan, 1991) because related diversification is the only expansion that accrues value to the firm (Rumelt, 1982).

This mechanism, competence re-use, has then an additional implication for the design of the present study. In a classic conceptualization where a radical technological shock is either fully competence-destroying or fully competence-enhancing for incumbents (Tushman and Anderson, 1986), only diversifying entrants or incumbents, respectively, have competences to re-use. The actual mix of competence destruction and re-use that both established firms enjoy in every disruption is masked. Therefore, decoupling market incumbency from organizational experience in creative destruction studies requires the measurement of the disruption to the R&D process in finer categories that capture different levels of competence destruction and re-use, taking the direction suggested by the most recent research into the characterization of technological disruptions (Gatignon, et al., 2002). In summary, I propose to not only decouple market incumbency from organizational experience in order to appropriately assign the disadvantage of organizational inertia, but also to measure in finer categories the levels of

competence destruction within the R&D process in order to appropriately assign the advantage of competence re-use.

### 3.5 A Summary of Mechanisms at Play

The presence of an advantage, beyond the disadvantage, stemming from organizational experience then completes the evolutionary picture. Firms fight for survival through the creation of specific competences, resource bases (Wernerfelt, 1984, 1995) that will support their reproducibility and capacity for the business at hand (Hannan and Freeman, 1989) in a pattern of “competition leads to competences” (Barney and Zajac, 1994, p. 6). Later, when faced with organizational change, established firms will face three different mechanisms.

The first mechanism is the *competence re-use* always present in established firms to different extents. It has been described for market incumbents (as competence enhancement [Tushman and Anderson, 1986; Gatignon et al., 2002]), and for diversifying entrants (Carroll et al., 1996), and it involves the advantage of having competences accrued through prior organizational experience that can now be re-utilized.

The competence destruction generated by a disruption to the status quo (whether such disruption is a change in technologies for incumbents or a change in markets for diversifying entrants) can be understood as two-fold.

On the one hand, it gives rise to *organizational inertia*, the second mechanism, which implies a “loss in efficiency,” because established firms are unable to identify some of the competences destroyed and hence keep attempting to use them when they are no longer appropriate (March and Simon, 1958; Cyert and March, 1963;

Burns and Stalker, 1966; Galbraith, 1973; Arrow, 1974; Nelson and Winter, 1982).

The inefficiency of *organizational inertia* has been described for incumbents (Henderson and Clark, 1990; Henderson, 1993), and for diversifying entrants (Mitchell and Singh, 1993).

On the other hand, established firms might be able to correctly identify some of the competences destroyed, and in those cases, they stop attempting to use them and instead start from scratch to build new competences. In this case, the firms only incur the loss of value of their destroyed resource bases without further loss of efficiency (i.e., without incurring inertia).<sup>17</sup> This then is the third mechanism, *new competence development*, which might be pursued in-house or acquired from other firms in a spot (acquisition) or relational (research alliance) transaction, but is nevertheless also always present. It has been described for incumbents (as competence acquisition<sup>18</sup> in [Gatignon, et al., 2002]) and for diversifying entrants (Roberts and Berry, 1985).

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<sup>17</sup> Note that we start to depart from the earlier analogy to “physical bodies.” Whereas Newtonian Mechanics would predict that a body always incurs inertia during change, it is, at least in theory, possible for an organization to incur no inertia during change. This feature, I believe, also “arises because organizations are more nearly decomposable into constituent parts than are [physical bodies]” (Hannan and Freeman, 1977, p. 934). Individuals and groups play a role inside organizations that have no parallel in “physical bodies.” Although all bodies in nature will incur inertia when facing change, organizations might, given the *agency* of the individuals inside them, avoid it. “Unlike the biotic case, in which membership in a population is encoded in *inert* genetic material, individual organizations can and sometimes do make radical transformations in strategy and structure” (Hannan and Freeman, 1989, p. 66, emphasis added).

<sup>18</sup> I refrain from using the term “competence acquisition” because it could give a sense of external acquisition, and the central part of the mechanism is actually that new competences should be developed. Whether the firm decides to outsource the development is a different matter (a matter of vertical integration).



In fact, devoid of *organizational-level* experience and its disadvantage, and of re-usable *firm-level* competences and their advantage,<sup>19</sup> de novo entrants are the only firm category dedicated entirely to new competence development.

The full picture of the underlying dynamics of competition is presented in Figure 3.4.

**FIGURE 3.4**  
**Underlying Dynamics of Competition**  
**during a Period of Technological Change**

	<b>Incumbents</b>	<b>Entrants</b>	
	<b>Established Firms</b>		<b>De Novo Firms</b>
	<b>Incumbents</b>	<b>Diversifying Entrants</b>	<b>De Novo Entrants</b>
<b>Competence Re-Use</b>	+	+	
<b>Inertia</b>	-	-	
<b>New Competence Development</b>	●	●	●

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<sup>19</sup> Note that the individuals working for de novo entrants, and for all three categories of firms under study, do have individual-level inertia and do have individual-level competences to re-use. The first effect was shown in a study of engineers by Allen and Marquis (1964), and is well known in experimental psychology settings (see, for example, “anchoring effects” in Tversky and Kahneman, 1982). The second effect has begun to receive attention. There is no evidence, however, that these effects are disproportionately present in the personnel employed either in incumbent, diversifying or de novo firms (I revisit this point in terms of the setting for this study in Chapter Five). Given the present state of our evidence, our only concern is in the difference between spinoffs and startups *within* the de novo category, which were noted in Klepper and Sleeper’s (2005) recent study. In it, the authors find that spinoffs have an advantage over startups, precisely because spinoffs do have organizational-level competences to re-use. As I will discuss in Chapter Five, this point actually shifts empirical results against the direction of my findings, and hence it does not constitute a challenge to results, but rather turns my statistical analyses into a conservative estimate.

The framework presented in Figure 3.4 supports then an additional proposition. As argued, the relevant firm categories to compare are not incumbents and entrants, but rather incumbents, diversifying and de novo firms. Yet in the absence of additional factors in the big picture of R&D and the underlying dynamics, if we had to compare only two categories of firms, it would not be incumbents vs. entrants, but established vs. de novo firms.

Once we realize that not every established firm characteristic is a disadvantage (i.e., inertia), we can also move away from asking why established firms try to compete, to asking why de novo firms try to do so.

Although de novo firms lack the advantage of competence re-use available only to established firms, they also lack the disadvantage. De novo firms do not have to make adaptation attempts in order to compete, attempts that are costly and uncertain (March, 1981; Hannan and Freeman, 1984, 1989). It is therefore rational for de novo firms to compete if they believe that despite their lack of advantages, they might outperform by their lack of disadvantages. It is the total sum of sources of competitive advantage and disadvantage that determines competition.

Another possible scenario is that both advantages and disadvantages might be deemed insignificant. Under such an assumption, all firms, established and de novo, would compete based on the pure differences in their abilities for new competence development, a competition that would then look like a pure R&D race.<sup>20</sup>

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<sup>20</sup> R&D races have been studied as patent races (where patent is the most immediate output of research and development) in the economic literature for a long time. The literature has compared pure races to races where an incumbent could have a first-mover advantage of any kind (e.g., Fudenberg, Gilbert, Stiglitz and Tirole, 1983).

The summary of underlying mechanisms presented in Figure 3.4 is therefore the theoretical framework I will use in the current study. It will guide the elements necessary for research design: three distinguishable categories of firms (incumbents, diversifying entrants and de novo firms), and distinguishable levels of competence destruction in the R&D process. This chapter hence moves away from absolute predictions, and offers instead a framework along the lines of former research in strategy formulation (Porter, 1991). Although based on the arguments presented in this chapter, an absolute prediction for the unraveling of competition is impossible to generalize (e.g., we might not know whether incumbents will lose or not in other disruptions based on the present market study), I certainly claim the framework to be generalizable.

## Chapter 4

### Empirical Setting:

### The Anti-Cancer Drug Market

#### 4.1 Selection Criteria for Empirical Setting

As explained in Chapter Three, I require two elements of research design for the present study: (1) presence of firms in the three firm categories of interest: incumbents, diversifying and de novo firms; and (2) measurement of different areas of R&D that vary in level of competence destruction.

Since the second criterion is a matter of measurement, I used the first criterion to judge different candidate markets for this research study.

As an additional criterion, I searched for a technological disruption that was currently taking place since that carried advantages in execution, including firm survival bias minimization and richer data collection. This choice makes this a *prospective* study, that is, a study in which the main end-point to measure, namely the final state of the market, has not yet taken place (Rothman, 2002). In contrast, the literature comprises only *retrospective* studies, that is, studies in which the final state of the market has been achieved. This difference carries advantages but also limitations, two of them important ones: the absence of the final distribution of market share after the period of radical technological change, and the differential evolution of research competence across categories of firms. The first limitation has

minimal impact due to my choice of R&D competence instead of market performance as the dependent variable. The second has a significant impact. It limits my ability to speak about the research competence of firm categories over the entire transition to the new technology. I can only conclude what the differences in research competence are *at this point* in the revolution.

The prospective nature of the present project also has an impact on the process of identifying a radical technological change for analysis. According to the literature, radical technological changes can be identified in two different ways. One is *retrospective*: look for a discontinuity in final product performance and trace it back to a radical change in the underlying science or technological competence (Tushman and Anderson, 1986). The other is *prospective*: directly identify a discontinuity or shift in the underlying science or technological competence used for research and development.<sup>21</sup> In the present prospective study, I identify the radical (i.e., competence-destroying for incumbents) disruption for study based on the requirement that the market undergoes a shift in the underlying science or technological paradigm used for research and development.<sup>22</sup> It is also important to

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<sup>21</sup> Tushman and Anderson (1986) explain that "... technological discontinuities [in terms of products that represent drastic changes in performance and that are finally adopted in the market]... are only known in retrospect..." (p. 443). In retrospective measurement, such discontinuities in performance can be traced back to competence-destroying technological changes for many markets. However, the authors discuss the definition of a technological change that is competence-destroying for incumbent firms by its own nature: "... [the fact that the new products] require new skills, abilities, and knowledge in both the development and production of the product" (p. 442).

<sup>22</sup> Furthermore, notice that what I require empirically is the assurance that the discontinuity is a shock to the R&D process, the focus of this study, regardless of whether a large increase in the price-performance ratio has already been achieved. In the case of the setting finally chosen, the market for anti-cancer drugs, the shift of technological paradigm that biotechnology represents is in fact already resulting in significant increases in final product performance (see, for example, the case of Gleevec's Phase III clinical trial results as reported by the National Cancer Institute at <http://www.nci.nih.gov/clinicaltrials/developments/newly-approved-treatments/page16>, visited on July 18, 2005). However, it is in theory still possible for the radical shift in technological paradigm that biotechnology represents not to result in drastic improvements in the average performance of products finally adopted in the market. This possible future divergence between the radical shift in

emphasize the fact that, prospectively, all definitions of radical innovation concur in describing it as requiring a new science, knowledge or technological paradigm (Dosi, 1982; Tushman and Anderson, 1986; Henderson and Clark, 1990).

I next briefly discuss two exemplary alternative settings considered and the reasons for discarding them, in order to then introduce the final setting of choice: the market for anti-cancer drugs.

## **4.2 Alternative Settings**

I considered and discarded alternative cases before finally selecting the market for anti-cancer drugs. Two particular examples are as follows.

### *4.2.1 The Revolution of Fuel Cell Energy Sources*

Although the engineering principles that constitute the basis of fuel cell energy sources were reportedly developed in the 19<sup>th</sup> century, the real uptake of the technology started in the 1960s.<sup>23</sup> The technology is meant to compete as a substitute for currently available energy sources, mainly gasoline and standard-means electricity. The revolution has developed five main variants: alkali, proton exchange membrane (PEM), molten carbonate, solid oxide, and phosphoric acid fuel cells.

Even though the five different technological variants would require the inclusion of control variables, and could render the comparison inconclusive, the main concern was with firm categories for analysis. Although the set of firms

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technological paradigm and the final product performance at the end of the disruption does not affect the internal validity of my present study as long as I can control for the presence of investment in each unit of time (i.e., as long as I can see if over the timeframe of my study, firms stopped investing in biotechnology if they realized this shift in technological paradigm would not bring about increases in final product performance).

<sup>23</sup> According to information from the Smithsonian Institute's project "Collecting the History of Fuel Cells" available at <http://americanhistory.si.edu/fuelcells/>, visited on April 11, 2006.

involved in fuel cell research certainly include firms of different sizes and ages, once broken down by market (where firms are in a market only if their products are substitutes for one another), some of the markets exhibit no entry, probably as a result of other market factors (e.g., capital intensity). In other cases, incumbent firms were difficult to identify since they are vertically integrated, that is, they produce their own components for internal consumption. In such cases, for example, identifying incumbents for the market for automotive engines was cumbersome because they were vertically integrated into automobile manufacturers. Table 4.1 displays the initial (rather incomplete) description of this market.

**TABLE 4.1**  
**Sub-Sample of Firm Categories present in Markets**  
**Disrupted by the Fuel Cell Energy Revolution**

Note: Incumbents are presented in black, diversifying entrants in blue, and de novo entrants in red.

Current Tech's	Market Niche	Alkaline / Zinc Air / Methanol / Other	PEM	Molten Carbonate	Solid Oxide	Phosphoric Acid
Central Power Plant, Small Gas Turbine, Diesel Genset, Wind	Fuel Cell, 250 kW – 25 MW, (Stationary power, Motive power)			Fuel Cell Energy, Ansaldo,	Siemens / Westinghouse, Acumentrics,	International Fuel Cell
Diesel Genset, Microturbine, Wind, Stirling Engine	Fuel Cell, 100 kW – 300 kW, (Stationary Microgrid)		International Fuel Cell, Ballard Power,	Fuel Cell Energy, MTU,	Siemens / Westinghouse, Acumentrics,	International Fuel Cell,
Internal Combustion, Electric / Microturbine	Fuel Cell, 150 kW – 250 kW, (Bus/Light Vehicle)	Eneco Ltd.,	General Motors, Ballard Power, International Fuel Cell, Axane Fuel Cell Systems,		Delphi Corp.,	International Fuel Cell,
Internal Combustion	Fuel Cell, 75 kW, (Automotive)	Aluminum Power [Al], Astris Transportation Systems Inc., EFFCELL GmbH, Eneco Ltd.,	General Motors / Toyota, International Fuel Cell, Ballard Power, Axane Fuel Cell Systems,		Global Thermoelectric, Delphi Corp.,	Bharat Heavy Electricals,
Grid Power, Flywheel, Stirling Engine, Battery, Solar	Fuel Cell, 1 kW – 5 kW, (Residential/UPS)	Metallic Power, Astris Energi, EFFCELL GmbH, EVionix,	International Fuel Cell, Plug Power, Ballard Power, Avista Labs, Nuvera, Idatech, Hydrogenics, Arcotronics Fuel Cells, Proton Energy [Regen.], Electrochem, Reliant Energy, APFCT, Clean Fuel Generation, Astris Transportation Systems Inc., Axane Fuel Cell Systems, Cellkraft, Baxi Group, Buderus AG, CEMIG,		Acumentrics, Global Thermoelectric, Sulzer Hexis, Matsushita Electric (Panasonic), Adelan Manufacturers, CERES Power, EBZ,	Apollo Energy Systems,
Battery, Flywheel, Solar	Fuel Cell, < 1 kW, (Portable/Micro)	Zinc: Metallic Power, Electric Fuel, Methanol: Mechanical Technology, Manhattan Scientific, MITI MicroFuel Cells, Neah Power, Direct Methanol Fuel Cells, Bee Power Systems, Other: AFS, Aluminum Power [Al], Angstrom Power,	Ballard Power, H-Power, Hydrogenics, Idatech, Electrochem, Giner Inc., Cellkraft, Element 1 Energy, Ball Aerospace & Technologies, CEAG AG, BCS Fuel Cells, Energy Conversion Devices,		Acumentrics, Adaptive Materials, Adelan Manufacturers,	
	Unknown application		Ecological Balances,		Advanced Power, CellTech Power, Altair International, Cummins Power Generation,	

Table 4.1 displays a sub-sample of all firms involved in fuel cell energy research as reported by *Fuel Cell Today* industry directory as of December 2003. Rows break down the sample into markets, and columns break down the market into technological variants. Firms are also color-coded by firm profile (i.e., incumbent, diversifying and de novo firm). Notice, for example, that no single row displays more than two or three incumbent firms.

#### 4.2.2 “Paper-like” Displays

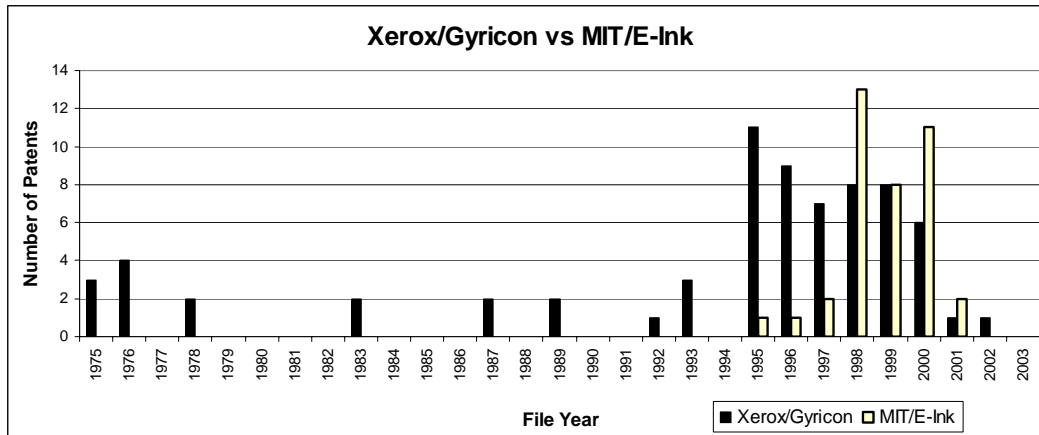
The founding of the startup E-Ink in 1997 and the official spin-off of Gyricon Media from Xerox Corp. in 2000 brought heightened attention to the development of a series of innovations that seemed to be giving birth to paper-thin displays, or what the media termed “electronic paper.” The idea of paper-like displays dated back to at least the 1970s. In May 1976, Nicholas K. Sheridan, the original Xerox scientist inventor of the Gyricon technology, applied for two patents already targeting “twisting ball panel displays,” the description of the Gyricon technology. Shelved within Xerox Corp. for two decades, it re-emerged along with competing new products in the 1990s (see Figure 4.1 for a timeline of patenting activity).

Although an interesting case of technological disruption, at the time of consideration, 2003, the only application tested by both firms for the current state of their technological development was supermarket signage. Substituting supermarket signage, that is, retail store displays, with electronic paper versions was estimated to reduce by \$250,000 per week the operating costs of department stores (Ditlea, 2001). How much of those savings could be appropriated by the firms as real revenue, and



how much of such latent revenue was dependent on subsequent possible changes in the product's features, was still unknown.

**FIGURE 4.1**  
**Number of Electronic Paper Patents**  
**Granted to Xerox/Gyricon and MIT/E-Ink**



Although supermarket signage surely represents a feasible stream of revenue, the top markets to target for significant profits were considered cell phone displays and even the uncertain “electronic newspaper.” For some applications, electronic paper seemed limited for technological reasons. Quite likely as a consequence of the either small or uncertain market size of the only current application, a broad search (through main industry publications and other sources) for firms competing in electronic paper technologies generated only eight firms in competition (see Table 4.2). Furthermore, “incumbents,” the firms who derived revenue from the market (or market segment) under threat (namely, manufacturers of supermarket signs) were not investing in the emerging technology, and the setting therefore lacked in-house R&D by incumbent firms. I discarded this setting because it offered a small and incomplete sample for study.

**TABLE 4.2**  
**Sample of Firms Competing in Electronic Paper as of 2003**

<b>Firm Name</b>	<b>Category</b>	<b>Source where found</b>
E-Ink Corp.	De Novo	<i>Scientific American, IEEE Spectrum</i>
Gyricon Inc.	De Novo	<i>Scientific American, IEEE Spectrum</i>
Zikon Corp.	De Novo	E-Ink patent citation
SiPix Imaging Inc.	De Novo	Other (online)
CPFilms Inc.	Diversifying	Other (online)
Kent Displays Inc.	De Novo	<i>IEEE Spectrum</i>
Stanley Electric Co. Ltd.	Diversifying	Other (online)
Papyron	De Novo	Other (online)

### 4.3 The Setting of Choice: The Market for Anti-Cancer Drugs

I discarded several other settings due to limitations on the sample required for study. Finally, I selected the market for anti-cancer drugs<sup>24</sup> and its transition from cytotoxic agents (i.e., antineoplastic antibiotics, alkylating agents, taxanes, etc.) to the radically new category termed targeted drugs (i.e., tyrosine kinase inhibitors, monoclonal antibodies, etc.), a transition brought about by the biotechnology revolution. This market offered the largest number of firms in competition, both total and per category of firms. It also offered a wealth of databases currently available that would support triangulation.

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<sup>24</sup> Note that economic theory defines products as being in the same market if they are substitutes for one another. Although confusion arises because cancer is a therapeutic category with several indications (e.g., breast cancer, lung cancer, etc.), where each indication has a separate line of treatment (i.e., a separate combination of surgery, radiotherapy and/or chemotherapy), each specific cancer indication does not constitute an independent market. Because an anti-cancer drug might treat several indications (e.g., Xeloda© is indicated for breast and colorectal cancer), even though it cannot treat them all (e.g., Xeloda© is not indicated in any of the leukemias), indications constitute “sub-markets” (Sutton, 1998) of the anti-cancer drug market. Many high-tech products constitute markets with sub-market fragmentation as reported for flowmeters (Sutton, 1998) or transistors (Tilton, 1971). According to Sutton (1998), although this market fragmentation does not invalidate the definition of the overall market, it certainly explains other economic irregularities. The most salient irregularity in these types of markets is the fact that although highly intensive in R&D expenditure, they exhibit low levels of market concentration.

As will be explained below, I operationalized this study through the selective use of archival data sources. Additionally, throughout the course of this project I interviewed 35 individuals, 4 of them repeatedly, with an evolving semi-structured interview guide, in order to clarify the use of data or to document examples of the present dynamics.

This setting has many advantages. It centers on a specific market (i.e., the products under study are substitutes for one another) in contrast to groundbreaking studies of the biotechnology revolution done at the industry level (e.g., Zucker, Darby, and Brewer, 1998). Additionally, the radical technological change in this study is a shock to the market but does not represent its birth, hence the presence of both incumbents and entrants, in contrast to studies where all firms are entrants since the shock marks the birth of the market (e.g., Carroll et al., 1996). The study focuses on research competence, and pharmaceuticals is the most research-intensive industry in the U.S. (PhRMA, 2003a), where research competence and resulting drug quality is a major determinant of profitability (Lu and Comanor, 1998). Finally, among therapeutic areas within pharmaceuticals, cancer research has the most new drugs in development (PhRMA, 2002) and an extremely large boom in commercial activity (PhRMA, 2003b).

Next, I describe my empirical strategy for identifying firms and firm categories (section 4.3.1). I then proceed to the characterization of the disruption to the R&D process and the identification of R&D sub-categories with differential levels of competence destruction (section 4.3.2). Lastly, I define the measurement of dependent and independent variables per sub-category of R&D (sections 4.3.3a, b and e). The discussion of operationalization includes two tests: a test for the

proportional nature of the separate samples (section 4.3.3c); and a test of the reliability of the drug ownership assignment to firms (section 4.3.3d).

#### 4.3.1 Identification of Firms and Firm Categories

I started by identifying the appropriate universe of firms. When selecting an incumbent firm for this study, I looked for a market incumbent that had decided to venture into the radically new category of targeted drug development.<sup>25</sup> By applying this restriction, I selected incumbents contingent on investment in the radically new technology, as set forth in Chapter Two (Figure 2.2).<sup>26</sup> Therefore, the universe of firms under study is composed of diversifying and de novo entrants and incumbents venturing into anti-cancer targeted drugs (a subset of all incumbents, termed simply incumbents hereafter for convenience).

To map this universe of firms, I used PJB Publications' database *Pharmaprojects*. I identified all anti-cancer drugs in clinical trials in the period 1989-2004 and then focused on the firms responsible for them. The search generated a list of 1,257 firms (responsible for a total of 6,177 different anti-cancer drugs) after excluding the National Institutes of Health (NIH) and a category for Non-Industrial Sources (that account for 205 and 469 additional anti-cancer drugs, respectively). In order to generate a sample that included firms with a clear intention to compete in the anti-cancer drug market,<sup>27</sup> I matched the 1,257 firms from *Pharmaprojects* to the firms reported in all available PhRMA Surveys *New Medicines in Development for Cancer*

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<sup>25</sup> Note that it is possible that with the advent of the new technology, an incumbent will opt for just "milking" the old technology for as long as possible and then exit the market.

<sup>26</sup> Furthermore, I control for the timing of entry in statistical analyses.

<sup>27</sup> That is, to avoid selecting firms that self-reported as working in cancer research but were rather committed only to a nearby area, such as AIDS or immunology in general.

(administered in 1988, and every two years from 1989 to 2003). This match generated a sample of 181 firms (14% of the total firms) responsible for 2,972 clinical trials (44% of the total anti-cancer drugs in clinical trials in *Pharmaprojects*). After I matched firms to their parent company to count only the latter, identified recent mergers and acquisitions up to the end of 2004, and discarded drugs with missing data, I identified the final sample, which comprises 165 firms (responsible for 2,281 anti-cancer drugs in clinical trials).

Next, I categorized firms as incumbents, diversifying or de novo entrants. Identifying the latter two categories was done through access to their corporate histories, culled mainly from their company websites. The major challenge was the identification of the relevant incumbent firms. These firms must have been present in the market for cytotoxic anti-cancer drugs before the era of biotechnology, and they must be venturing into targeted anti-cancer drugs now. Since the era of chemotherapy (i.e., cytotoxic anti-cancer drugs) in cancer treatment started in the 1940s (Chabner and Roberts, 2005), most records are incomplete.<sup>28</sup> I therefore triangulated three different sources to identify incumbent firms: the records available from the Federal Drug Administration (FDA) on all approved drugs;<sup>29</sup> the records available on anti-cancer drugs in particular from the FDA's Center for Drug

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<sup>28</sup> For example, FDA records for drug approval are partially incomplete before 1982, likely because they are prior to the approval of the Drug Price Competition and Patent Term Restoration Act of 1984 [the Hatch-Waxman Act], which gave rise to today's generics drug industry.

<sup>29</sup> From [Drugs@FDA](mailto:Drugs@FDA) available electronically at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>

Evaluation and Research (FDA-CDER);<sup>30</sup> and the printed collection of the *Physician Desk Reference* (PDR) drug directories for the years 1947-2005.<sup>31</sup>

I took the approval of the first anti-cancer drug influenced by biotechnology, *Intron-A*® (a recombinant-DNA molecule) introduced by Schering-Plough in 1983, as the start of the era of targeted anti-cancer drugs.<sup>32</sup> An incumbent therefore would be a firm that was present in the market before 1983 and that after 1983 has at least one targeted anti-cancer drug either in clinical trials or already launched. Firms that were in the market but left for a significant period of time and are now returning because of the biotechnology revolution are not incumbents but diversifying entrants.<sup>33</sup> I therefore further corroborated the presence of the firms around 1983 by requiring that at least one of the cytotoxic anti-cancer drugs for the firm in question still generated revenue after 1983. I estimated this through one of two available proxies: at least one of the cytotoxic anti-cancer drugs for the firm in

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<sup>30</sup> From FDA-CDER Oncology Tools available electronically at <http://www.fda.gov/cder/cancer/druglistframe.htm>

<sup>31</sup> The PDR collection generated the richest list of drugs related to cancer (406 drugs). After discarding targeted anti-cancer drugs and drugs with low cross-elasticity of demand to cancer treatment (e.g., pain killers such as codeine listed in the PDR as indicated for a long list of uses beyond cancer treatment), I documented 146 cytotoxic drugs corresponding to 36 different parent firms, which I then cross-referenced with the FDA and FDA-CDER sources. Many of these firms have either left the anti-cancer drugs market and to date have not re-entered (e.g., Hynson, Westcott & Dunning), or have consolidated through later mergers and acquisitions (e.g., Sterling Winthrop, acquired by Kodak, and later by the firm today known as Sanofi-Aventis).

<sup>32</sup> Although *Intron-A*® is approved for indications other than cancer and is reported in the FDA-CDER Oncology Tools only after 1997, it is listed as an Antineoplastic (i.e., anti-cancer drug) in the PDR manual (of wider use among the medical community than FDA-CDER Oncology Tools) starting in 1987. For all other drugs in this study, the PDR manual reported a lag of 2 years from start of use, and therefore, the starting point for the biotechnology revolution in the anti-cancer drug market can be reliably estimated as sometime between 1983-1985. Use of any year in that window does not alter the definition of incumbent firms for the present analysis. Furthermore, expert interviewees supported the reliability of this choice.

<sup>33</sup> For example, Merck made two attempts to enter the anti-cancer drugs market with Nitrogen Mustards *Mustargen*® and *Cosmegen*® in the years 1949 and 1966, respectively, but was by 1983 long gone from the market. Neither product had significant sales after 1983 (as shown by their absence from the *Med Ad News Top 500 Prescription Drugs* reports 1991-2002 and their lack of generic introduction after 1984). *Cosmegen* is even reported as unprofitable in Merck's Annual Report in 1951. Now that Merck is attempting to enter the anti-cancer drugs market again, it is classified as a diversifying entrant.

question must have had revenues listed in the *Med Ad News*' yearly report of Top Prescription Drugs in the period 1991-2002, or must have had a generic introduction after the generics industry took off in 1984 as reported in the PDR collection.<sup>34</sup> The decision tree followed for the categorization of firms as incumbents, diversifying entrants or de novo entrants, including data sources accessed, is depicted in Figure 4.2.

The sample of 165 firms therefore comprises the following: 8 incumbents, a list that is exhaustive; 44 diversifying entrants; and 113 de novo entrants. The latter two categories of firms are not exhaustive but rather representative samples.<sup>35</sup>

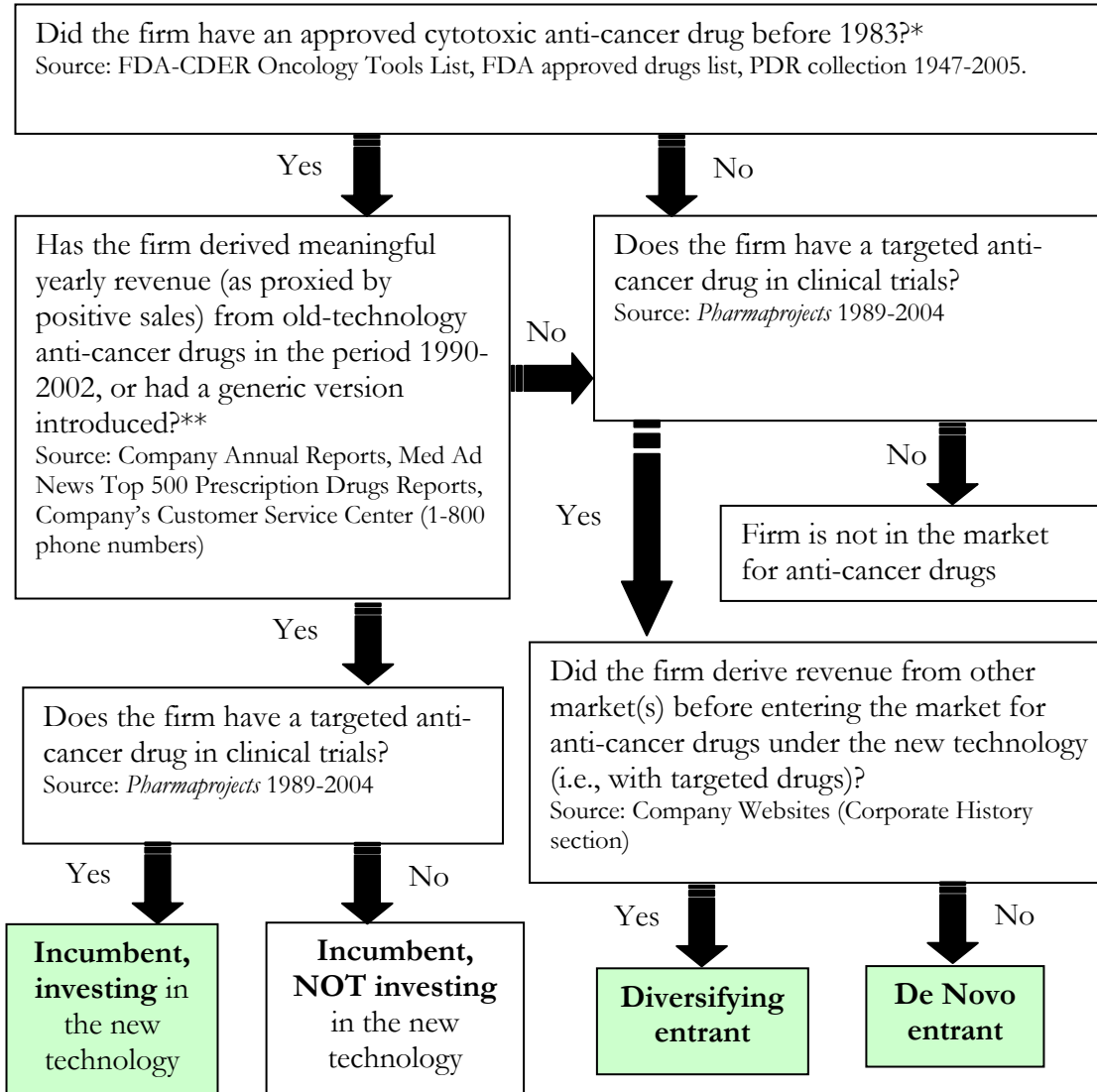
It is important to clarify that the category of incumbents does not coincide with the firms popularly known in this industry as “big pharma.” Incumbents in this study are market-level incumbents. “Big pharma” are a subset of industry-level incumbents. They appear in this study only if they were present in the anti-cancer drug market before biotechnology (in which case they appear as incumbents) or if they are now entering the anti-cancer drug market in the transition to biotechnology (in which case they appear as diversifying entrants).

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<sup>34</sup> I assume that only anti-cancer drugs with positive revenues will incite generic competition.

<sup>35</sup> The unbalanced nature of this panel, especially the small number of incumbents, is a key characteristic of the phenomenon of creative destruction. Since, by definition, incumbents have been in the market for a long period (prior to the transition to the new technology), they underwent a period of market consolidation and exit typical of any path of maturation for a given technology in a given market (regardless of the explanatory mechanism proposed, scholars consistently report the empirical regularity that markets consolidate as they mature, see Klepper and Graddy, 1990; Utterback, 1994; Jovanovic and MacDonald, 1994).

**FIGURE 4.2**  
**Decision Tree to Categorize Firms**



\* This requirement ensures that the firm was an incumbent to the market prior to its investment in new-technology anti-cancer drugs (as opposed to just deciding to enter the market investing in both old and new technologies in parallel). The year 1983 was when the first Targeted Anti-Cancer Drug was launched on the market, and I therefore use it as a milestone.

\*\* This requirement ensures that the firm did not leave the market and come back to it because of the new technology's effect on lowering barriers to entry. If a firm exits a market before the transition due to the radical technological change starts, then that firm is not in the market at the time of the radical change and therefore is not an incumbent. If it stays away from the market, then it is out of the scope of relevance for this study. If it comes back after several years, investing in the new technology, then it is a diversifying entrant.



### 4.3.2 Characterization of the Disruption to the R&D Process

In order to analyze the technological disruption in multiple categories rather than a binary of full competence-destruction or full competence-enhancement, I first offer a more elaborate picture of the impact of the biotechnology revolution on anti-cancer drug development. The idea is to follow the measurement of firm competences in the *smallest number* of relevant categories that capture the gist of the variance in competence destruction (Gatignon et al., 2002).<sup>36</sup> Based on interview material with scientists and clinical oncologists, I document the biotechnology disruption to anti-cancer drug development as taking place in two directions: the mechanism of action of the drug, and the molecule size (see Figure 4.3).

**FIGURE 4.3**  
**The Effect of the Biotechnology Disruption**  
**on Anti-Cancer Drug Development**

		Mechanisms			
		Cytotoxic *	Targeted		
			TK inhibitors	Anti-angiogenesis	etc.
Molecule Size	Small molecules	Old Technology	New Technology	New Technology	New Technology
	Large molecules	X	New Technology	New Technology	New Technology

\* Although producing a cytotoxic large molecule anti-cancer drug is technically feasible, it is economically impractical since cytotoxic anti-cancer drugs are expected to be of lower quality in the long-run, and large molecules are significantly more expensive to mass-produce than small molecules (in the estimated order of 50:1 according to interview material).

<sup>36</sup> The proposition in Gatignon et al., (2002) is to use survey data and find a more detailed measurement for key characteristics of the disruption dynamics. However, I departed from that specific design due to my decision to make R&D competence the dependent variable (instead of the independent variable as is common). I therefore identified instead the minimum number of categories in the R&D process that can be used to capture the gist of the variance in levels of competence destruction. This is closer to the methodology used in Burgelman's (1994) study of innovation at Intel, notwithstanding the fact that this classic study implemented categories for the entire innovation process, not only R&D.

Considering these directions, I classify the level of competence disruption (i.e., the mix of competence destruction and enhancement) in three relevant sub-categories: preclinical drug design, manufacturing process design, and the execution of clinical trials (see Figure 4.4).<sup>37</sup> Notice that at this point in the biotechnology revolution interviewees described clinical trial execution as largely undisrupted although they do report that significant changes are starting to take place (e.g., the use of biomarkers in clinical trials [Arteaga and Baselga, 2004]).

The description of biotechnology's impact on the market for anti-cancer drugs that I present in Figure 4.4 is consistent with industry-level descriptions of this "revolution." Henderson, Pisano and Orsenigo (1999) describe a distinguishable

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<sup>37</sup> Two crucial questions are raised once the process for anti-cancer drug development (anti-cancer drug R&D process) is broken down into these three categories: (1) are manufacturing process design and clinical trials execution part of the R&D process or of the commercialization process (mainly, as a complementary asset for commercialization)?; and (2) is anti-cancer drug clinical trials execution a firm-specific competence even though clinical trial execution is frequently outsourced in the pharmaceutical industry?

To answer the first question, complementary assets are defined as mediating factors between the successful *completion* of the R&D process and the appropriation of rents (Teece, 1986). Installed manufacturing capacity (and its reliable functioning) and marketing efforts are common complementary assets in pharmaceuticals (and commonly mediate in the appropriation of rents, such as the case of Chiron's shortage of flu vaccine production [*Financial Times*, 2004] and the famous debate on higher marketing than R&D expenses in pharmaceuticals [U.S. Congress, Office of Technology Assessment, 1993]). Still, manufacturing process *design* and clinical trials execution are not complementary assets. The design of manufacturing processes is a standard component of R&D in any industry and has long been argued to need parallel coordination with product design in the product development literature (e.g., Graves, 1989; Ha and Porteus, 1995). In addition, prior to clinical trials, the patented molecules identified as drug candidates remain only that, candidates. As a standard, the process of clinical trials will discard approximately 80% of drug candidates as ineffective or unsafe for use in humans (PhRMA, 2003a).

To answer the second question, notice first that it is only recently that the execution of clinical trials has achieved a larger proportion of outsourcing (prior to 1996 it is estimated that only 8.5% of all clinical trials was outsourced [Azoulay, 2004]). Second, cancer as a therapeutic category is one of the least outsourced areas in terms of clinical trials (with a mean outsourcing level of 10.3% in the period 1995-1999, second only to ophthalmology [Azoulay, 2004]). Furthermore, even if clinical trial execution were outsourced, this competence is still firm-specific unless carried out in a spot-transaction manner (relational transactions with specific suppliers do represent a firm-specific competence). Interview material reveals that pharmaceutical firms do hold a list of preferred clinical trials execution suppliers (named Contract Research Organizations or CROs), and therefore engage in relational transactions. Furthermore, there is evidence that working repeatedly with a CRO does benefit the firm contracting the service (Boerner, 2002). Unfortunately, the standard source of information for clinical trials outsourcing, Fast Track Systems' CROCAS database, does not allow quantitative assessment of the frequency of switching among suppliers by outsourcing pharmaceutical firms.

difference between the impact to drug development and to process design.

Rothaermel (2001, p.691) qualifies the impact of biotechnology on the part of the drug development process that I here term “preclinical drug design” as full competence destruction for incumbents, at least in the area of scientists’ skills.

**FIGURE 4.4**  
**The Disruption of Biotechnology to**  
**the Sub-categories of Competence within Anti-Cancer Drug Development**

Firm competence	Type of drug		
	Cytotoxic drugs (always small molecule)	Targeted small molecule	Targeted large molecule
Preclinical Drug Design	Baseline	Disrupted	Disrupted
Manufacturing Process Design	Baseline	Not Disrupted	Disrupted
Execution of Clinical Trials	Baseline	Not Disrupted	Not Disrupted

Note: Notice that the baseline of the disruption is the list of competences required to develop cytotoxic drugs and the state-of-the-art of R&D in this market up to the moment when the period of radical technological change began. It is against that baseline that the competences required to perform the different steps of R&D for targeted anti-cancer drugs, whether small or large molecule, are measured. For example, because designing the manufacturing process for targeted *small* molecule anti-cancer drugs is done in basically the same manner as for cytotoxic anti-cancer drugs, that cell reads “Not Disrupted.” Because designing the manufacturing process for targeted *large* molecule anti-cancer drugs is done in an entirely different way (i.e., recombinant DNA and fermentation technology), that cell reads “Disrupted.”

Based on this operationalization, my proposition implies moving away from the usual 1X2 design<sup>38</sup> in creative destruction studies on R&D and into a 3X3 design<sup>39</sup> (see Figures 4.5a and 4.5b).

As can be readily seen, the analysis of a 3X3 design is extremely cumbersome. I take advantage of the fact that the sub-categories of competence destruction constitute not just a categorical but an *ordinal* variable (a variable that measures low, medium and high levels of disruption, for preclinical drug design,

<sup>38</sup> This means a design with 1 factor (populations of firms) and 2 levels (incumbents and entrants). That is, this is a 2<sup>1</sup> quasi-experiment in factorial design, with 2 cells in total for comparative analysis.

<sup>39</sup> This means a design with 2 factors (firm populations and disruption levels) and 3 levels per factor (3 populations of firms and 3 levels of disruption to the R&D process). That is, this is a 3<sup>2</sup> quasi-experiment in factorial design, with 9 cells in total for comparative analysis.

manufacturing process design and the execution of clinical trials, respectively). I therefore separate the statistical analyses of the differences in these competences into two chapters. In Chapter Five, I concentrate on the contrast between low and high levels of disruption (i.e., the area with full competence destruction and the area with full competence re-use for incumbents, see Figure 4.5c). I defer to Chapter Six the statistical analysis of differences in competence in manufacturing process design.

**FIGURE 4.5**  
**Standard Design of Studies on the Impact of Creative Destruction on R&D and the Design of the Current Project**

(4.5a). 1X2 standard design of studies on the impact of Creative Destruction on the R&D process

		<i>Firm Categories</i>	
		Incumbents	Entrants
R&D Process	High		
	Low		

(4.5b). 3X3 design resulting from the research elements proposed in this study and the specifics of the setting of choice

<i>Levels of Disruption</i>		<i>Firm Categories</i>		
		Incumbents	Diversifying Entrants	De Novo Entrants
High =	Preclinical Drug Design			
	Manufacturing Process Design			
Low =	Execution of Clinical Trials			

(4.5c). 2X3 design adopted for analysis in Chapter Five.

<i>Levels of Disruption</i>		<i>Firm Categories</i>		
		Incumbents	Diversifying Entrants	De Novo Entrants
High =	Preclinical Drug Design			
	Execution of Clinical Trials			

Clearly, distinguishing between targeted small molecules and targeted large molecules is only particularly relevant for the analysis of competence disruption for manufacturing process design.<sup>40</sup> Therefore, in analyses in Chapter Five, I distinguish only between cytotoxic and targeted drugs. In analyses in Chapter Six, however, I return to the analysis of manufacturing process design and hence to the original distinction to separate targeted small molecule from targeted large molecule drugs.

#### *4.3.3 Measurement of Research Competence in each Sub-category*

In order to measure the R&D competence in each level of disruption across categories of firms, I make use of three different dependent variables and therefore of three different main datasets.

##### *(a) Research Competence in Preclinical Drug Design*

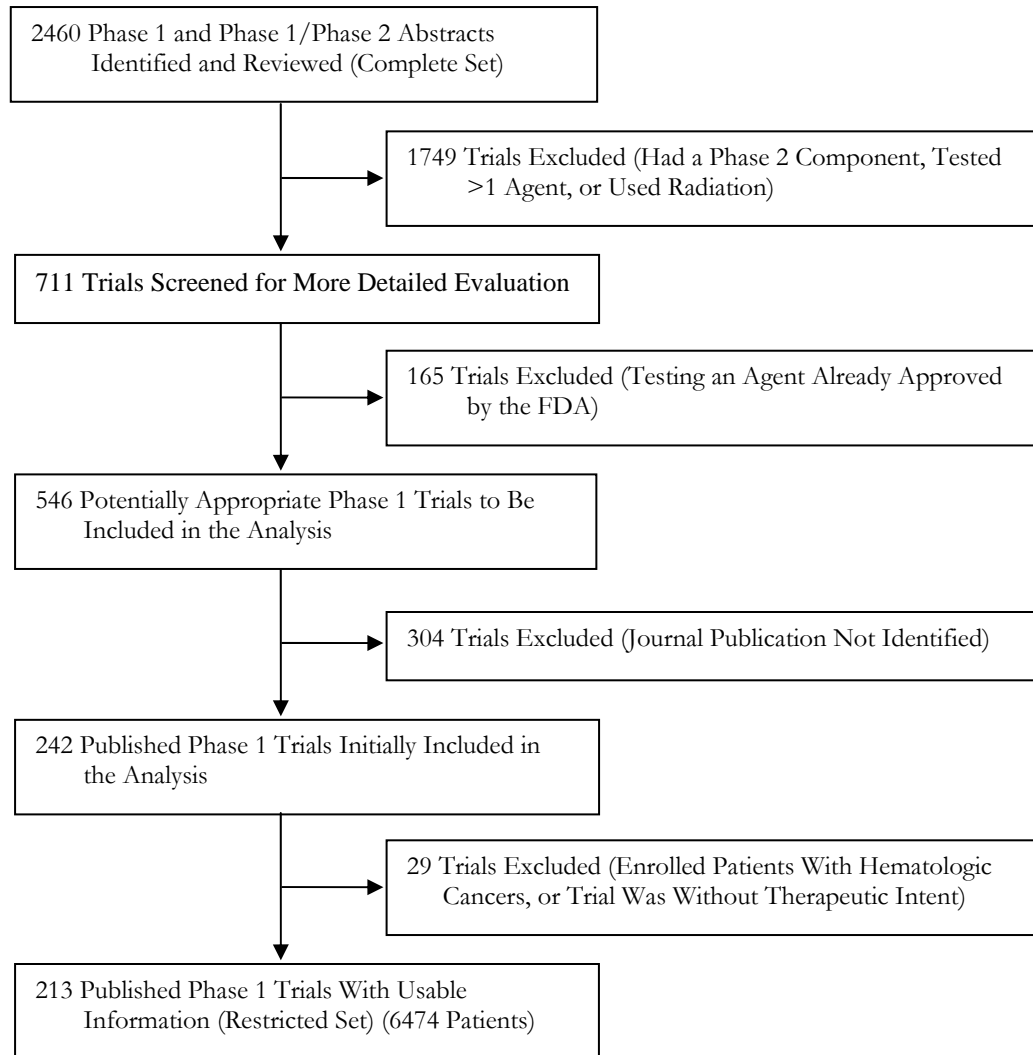
I assessed differences across categories of firms in their competence in preclinical drug design through information on phase I trial results for anti-cancer drugs documented in the American Society of Clinical Oncologists' (ASCO) Proceedings in the period 1991-2002, a dataset originally published in Roberts et al., (2004).<sup>41</sup> I matched drugs to the firms originating them as reported in the *Pharmaprojects* database. I started with the sample of 213 phase I trials originally analyzed in Roberts et al., (2004) (see Figure 4.6 for a replicate of the selection process of these 213 phase I cancer trials out of the 2460 phase I cancer trials identified through ASCO Abstracts, as reported in the original).

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<sup>40</sup> That is, Figure 4.4 only posits a clear change in disruption between targeted small molecules and targeted large molecules in that competence.

<sup>41</sup> I gratefully acknowledge full access to the dataset from the original authors, especially Thomas Roberts, M.D., Bernardo Goulart, M.D., Stan Finkelstein, M.D., and Jeffrey Clark, M.D.

**FIGURE 4.6**  
**Replicate of “Figure 1. Trial Flow Used in Identifying Studies for Detailed Analysis” from Roberts et al., (2004), p.2133**

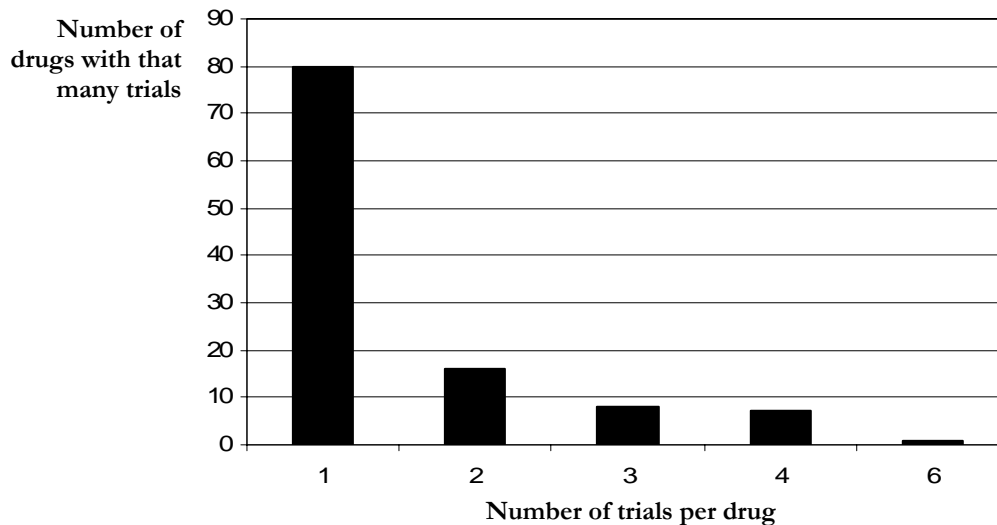


I was then able to find a match for 187 (87.8%) trials.<sup>42</sup> I discarded 15 trials because the originator of the drug is a non-profit organization and ended with a sample of 172 phase I trials. Whereas the original 213 trials corresponded to 149 unique drugs in Roberts et al., (2004), my final sample of 172 trials corresponds to

<sup>42</sup> The remaining 26 (12.2%) trials lack information to permit a match to its originating firm (e.g., the publication reports the anti-cancer drug only in mentioning its broader drug class, such as *a* GM-CSF or *an* Interleukin-2).

113 unique drugs. Although I use the anti-cancer drugs to infer the performance of the firms that originated them, the unit of statistical analysis in this section remains the trial. This is the case because trials that have a drug in common differ in their measures for control variables (to be described next) and hence could not be aggregated. Figure 4.7 shows the distribution of number of trials per drug in the dataset. In statistical analyses for this competence (Chapter Five) I control for replicate trials in all models either through a dummy variable or by clustering standard errors around trials sharing the same drug.

**FIGURE 4.7**  
**Distribution of Replicate Trials per Unique Drug in the Final Sample for Measurement of Competence in Preclinical Drug Design**



I use this dataset to perform regression analysis on response rate during the phase I trial.<sup>43</sup> Response rate is measured as the proportion of patients enrolled in the trial who exhibit a reduction in the size of their tumor. I use this variable as a

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<sup>43</sup> Cancer is the only therapeutic category in which phase I trials recruit diagnosed patients and not healthy volunteers, although recruited patients can have any type of tumor. It is also the only therapeutic category in which randomized trials are never tested against placebos but rather against benchmark treatments by regulation.

proxy for drug quality.<sup>44</sup> In addition to variables to identify the three categories of firms (with *de novo* as the omitted category), I differentiate cytotoxic and targeted anti-cancer drugs. To construct the variable “Targeted,” I measured its two subclasses of drugs: targeted *small* molecules and targeted *large* molecules (the latter also commonly referred to as “biologics” or “biopharmaceuticals”). The identification of the latter is reliably documented in the *Pharmaprojects* database. It is the targeted small molecules that are difficult to identify since they are in many ways (e.g., molecular weight) similar to cytotoxic drugs. The main difference between them is that they were discovered through a process of “mechanism-driven” development.<sup>45</sup> I therefore selected all drugs with mechanisms of action described in industry reports (e.g., Bear Sterns, 2002; Stephens Inc., 2002; UBS Warburg, 2001) as “mechanism-driven” within anti-cancer drug development and identified them as targeted small molecules (in the end, mainly comprising angiogenesis and kinase inhibitors).

I also include as a control the variable “Two or fewer Tumor Types,” a binary variable that represents the number of different indications (e.g., breast cancer, lung cancer, etc.) included in the trial. This variable is necessary because greater numbers of tumor types are significantly associated with lower trial efficacy, as shown in the original Roberts et al., (2004) and in interview material. Lastly, I include the death rate per clinical trial and its interaction with “Targeted” as controls

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<sup>44</sup> Response rates in cancer phase I trials can be argued to measure two firm capabilities together, that of designing the drug with high quality (efficacy) and that of designing the phase I trial itself, with no way to discern between them. Still, there is evidence that higher response rates in cancer phase I trials are significantly related to better results in subsequent phase III trials (Sekine et al., 2002), which supports the construct validity of my intended use for this proxy.

<sup>45</sup> Strictly speaking, I am looking to differentiate between randomly designed drugs and mechanism-driven designed drugs. Although all targeted large molecule drugs are mechanism-driven designed drugs, targeted small molecule drugs need not be. A targeted small molecule drug can be designed randomly and only afterwards have its target discovered. It is in this sense that my definition of cytotoxic vs. targeted differs slightly from that used originally in Roberts, et al., (2004), in which the authors defined targeted strictly as having a target.



as well. Death rate is measured as the proportion of patients enrolled in the trial who died due to toxicity.

(b) *Research Competence in Preclinical Drug Design and Clinical Trial Execution*

I implement the innovative differentiation of levels of disruption within R&D not without caveats. Although ideally I would have measured each competence independently, the sequential nature of the two steps of preclinical drug design and clinical trial execution makes the measure of firm competence in each step necessarily nested. That is, I measure differences across categories of firms in their competence in preclinical drug design alone according to section 4.3.3(a). But I measure differences across categories of firms in their competence in clinical trial execution *and* preclinical drug design jointly.<sup>46</sup> It is not until I compare the analyses of the two datasets that I can draw conclusions about preclinical and clinical competences separately.

I assessed differences across categories of firms in the competences of preclinical drug design and clinical trial execution jointly directly through the *Pharmaprojects* database. I identify when each drug entered and exited clinical trials, and whether the drug was ultimately approved (or if it is still in clinical trials or was discontinued, in which cases I treat them as right-censored).<sup>47</sup> I use this dataset to perform event history analysis. Because the dates in *Pharmaprojects* are detailed down

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<sup>46</sup> Although the ability of a firm to competently execute a clinical trial makes a significant difference in the advancement toward drug approval, so does the actual quality of the drug. If advancing toward drug approval depended only on the competence of executing clinical trials, a “skillful” firm could get a placebo approved for cancer treatment, a fact well known to be impossible.

<sup>47</sup> Although information on a competing event, the discontinuation of clinical trials, was also available, it could not be disaggregated into trials discontinued at the recommendation of the FDA or leading oncologists in charge of the trial, and those discontinued at the discretion of the sponsoring firm (this latter constitutes a firm-specific capability). Without disaggregating the two cases, no conclusions can be inferred, and therefore, I consider only drug approvals in my analysis.

to the day, month and year (i.e., detailed enough to avoid tied events), I interpret the data as a continuous-time event occurrence and select Cox Models for their analysis (Singer and Willett, 2003). Cox Models are non-parametric and therefore impose the least assumptions on the data. I again use the same variables to identify the three categories of firms and the distinction between cytotoxic and targeted drugs. I include further controls (partly thanks to the larger size of the dataset) for firm age and size and for the cumulative introduction of drugs into clinical trials by each firm category (variable “Cumulative”). Furthermore, I control for the “novelty” of the drug. The variable “Drug Novelty” is defined as the inverse of the chronological place of introduction that the drug holds on the list of drugs within the same mechanism of action (a replicate of the measure included in Guedj and Scharfstein, 2004). Finally, I control for the presence of an R&D Alliance through a dummy variable with value 1 if the drug had an R&D alliance associated with it reported in the cancer sub-section of the *Windhover’s Pharmaceutical Strategic Alliances* collection 1986-2003.

Lastly, it is important to mention another source of variance controlled by the design of this sample. The recent literature (Guedj and Scharfstein, 2004) has argued that firms with 3 or fewer drugs in their portfolios have distorted behavior since, lacking other viable projects, they become significantly resistant to kill underperforming projects. In the 165-firm sample I identified, only 14 firms have 3 or fewer drugs throughout the observation period. Because 13 out of those 14 are de novo firms, I consider this distortion not only small, but as will be seen, also as working against results (i.e., making it a conservative test). I therefore judged unnecessary to include a control variable on this respect.

(c) *Comparison of the two Main Data Sources used for Joint Analysis*

In order to draw conclusions about the set of 165 firms identified as competing in the anti-cancer drug market, through the comparison of two independent samples of their drugs under development (i.e., the 113-drug sample and the 2,281-drug sample), I needed to test the comparable proportions of these two samples. For this purpose, I built a matrix with the counts of drugs in each of the six classes resulting from all combinations of the three categories of firms and the two technologies (i.e., cytotoxic drugs from incumbents, targeted drugs from incumbents, cytotoxic drugs from diversifying entrants, and so forth) for the 113-drug sample vs. the 2281-drug sample. This process generated a 6X2 matrix in which to test differences in proportions, as displayed in Table 4.3.

**TABLE 4.3**  
**Comparison between 113-Drug Sample and 2,281-Drug Sample**

*Distribution of Types of Drugs  
across Firm Categories for the Two Samples*

	Incumbent		Diversifying Entrant		De Novo	
	Cytotoxic	Targeted	Cytotoxic	Targeted	Cytotoxic	Targeted
113-drug sample	20	13	31	14	18	17
2,281-drug sample	337	162	510	354	443	475

The Pearson Chi<sup>2</sup> test for differences in the distribution of proportions across the two samples is not significant (Pearson chi<sup>2</sup>[5] = 7.8, p < 0.17). The lack of significance means that the proportions across the six classes are comparable in each sample. This result supports the representative nature of one sample vs. the other and allows me to use them in joint statistical analysis.

(d) *Testing the Reliability of Drug Assignment to Firms*

Because the assignment of drugs to their originating firms is crucial for analysis, I further test the reliability of this information. *Pharmaprojects* reports for some drugs the number for the patent of the actual drug molecule. Of the 2,281 drugs, 419 have a patent reported for them.<sup>48</sup> Although this 419-drug sub-sample was not randomly selected, but rather the result of missing data, it is representative of the proportions of incumbents, diversifying and de novo entrants in the larger 2,281-drug sample (Pearson  $\chi^2[2] = 0.84$ ,  $p < 0.65$ ).

A potential challenge to the use of the originator firms reported in *Pharmaprojects* is the possibility that incumbents conduct disproportionately more drug acquisitions from the other firm categories, because they are the firms at risk of underperforming in preclinical drug design. Intense drug acquisition would improve their performance measure in this R&D sub-category, but it would not reflect in-house research competence.

The reliability of the firm name reported originally in *Pharmaprojects* is supported as 291 of the 419 patents (69.5%) have the same assignee as the firm listed as originator in the analysis.

Furthermore, Table 4.4 shows the distribution of types of drug owners and corresponding patent assignees for the 128 patents (30.5%) whose assignee is different from the firm reported as owner in *Pharmaprojects*. Contrary to expectations, incumbents are the least present category within this 128-patent sub-sample (only

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<sup>48</sup> Searching for patents for drug molecules is significantly difficult. An expert interviewee examined sample patents from this 419-patent list and corroborated their nature as patents for drug molecules (as opposed to use patents). Still, my attempt to expand the current sample even when supported by the MIT Technology Licensing Office's expert personnel proved extremely time- and resource-consuming and rendered the task impractical.

18% of the drugs mismatching originating firm and patent assignee have an incumbent as a firm). The highest proportion is of de novo firms (50%), with diversifying entrants in second place (32%). Although firms acquire drugs in equal proportions from for-profit and not-for-profit organizations (48.4% vs. 51.6% accordingly), the pattern is not random (Pearson  $\chi^2[2] = 17.73$ ,  $p < 0.0001$ ) and is led by de novo firms acquiring drugs from universities. This pattern probably reflects the common dynamics of entrepreneurship within biotechnology, which is heavily based on technology transfer out of university laboratories (Murray, 2002).

**TABLE 4.4**  
**Types of Drug Owners and Patent Assignees for Mismatching Cases**  
**(N = 128)**  
*All counts are patents*

Category for Drug Owner	Category for Assignee in Patent for Drug Molecule							TOTAL
	For-Profit Organizations (n <sub>1</sub> = 62)				Not-for-Profit Organizations (n <sub>2</sub> = 66)			
	Incumbent	Diversifying Entrant	De Novo Entrant	Unclassified Firm	University	Research Center	Other (mainly Government)	
Incumbent	0	15	1	4	2	1	0	23 (18%)
Diversifying Entrant	0	14	1	4	11	7	4	41 (32%)
De Novo Entrant	7	10	3	3	28	11	2	64 (50%)
TOTAL	7	39	5	11	41	19	6	128 (100%)

(e) *Research Competence in Manufacturing Process Design*

Finally, I assess differences across the three firm categories in their competence in designing manufacturing processes through the use of a dataset of process patents acquired from the *Thomson Derwent World Patent Index* collection. Because only the design of manufacturing processes for targeted large-molecule drugs is disrupted (refer back to Figure 4.4), I look specifically at these processes only, commonly known as rDNA/fermentation technology processes. The dataset contains then all rDNA/fermentation technology process patents assigned to the 165 firms identified in the sample for this study. In order to collect only rDNA/fermentation technology process patents, I took all *Thomson Derwent* codes under the umbrella “Processes, Apparatus” and asked expert interviewees to perform the selection of relevant codes.<sup>49</sup> The resulting set of 4 specific *Thomson Derwent* codes paired with the 165 firms in the sample generated a dataset of 1,376 patents. Although the *Thomson Derwent World Patent Index* collection spans the years 1963-2005, the 1,376 patent sample spans the years 1986-2005 (for patent publication date) only.

Notice the different nature of this dataset, as compared to those used to assess research competence in preclinical drug design and clinical trial execution described above. These latter datasets were built by selecting all anti-cancer drugs, with or without biotechnology influence (i.e., cytotoxic as well as targeted), for the 165 firms in the sample. The present dataset, in contrast, was built by selecting all process patents with biotechnology influence, with or without relation to anti-cancer drug development, for the same firms. This process of data collection will therefore

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<sup>49</sup> Special thanks to Samuel Ngai, for his detailed assessment of the 69 process codes under the umbrella of “Processes, Apparatus.”

impose different conditions of analysis for the manufacturing process design dataset. While the datasets for preclinical drug design and clinical trial execution can be analyzed either stratified into old vs. new technology or in full with a technology interaction term, the dataset for process design is stratified on the new technology by design. Because the discourse is on incumbents' competence in the research of the *new* technology, lacking access to the old technology performance is a limitation but does not destroy the internal validity of the test. Additional to variables identifying the three firm categories, I include controls for firm age and size, and the cumulative level of patenting per firm category. I use event-history analysis to model the rate of patenting over time using a Cox Model as available previously in the literature (Sørensen and Stuart, 2000).

## Chapter 5

# Decoupling Market Incumbency from Organizational Experience

## An Analysis of Preclinical and Clinical Competences

### 5.1 Categories of Firms and their Distributions of Size and Age

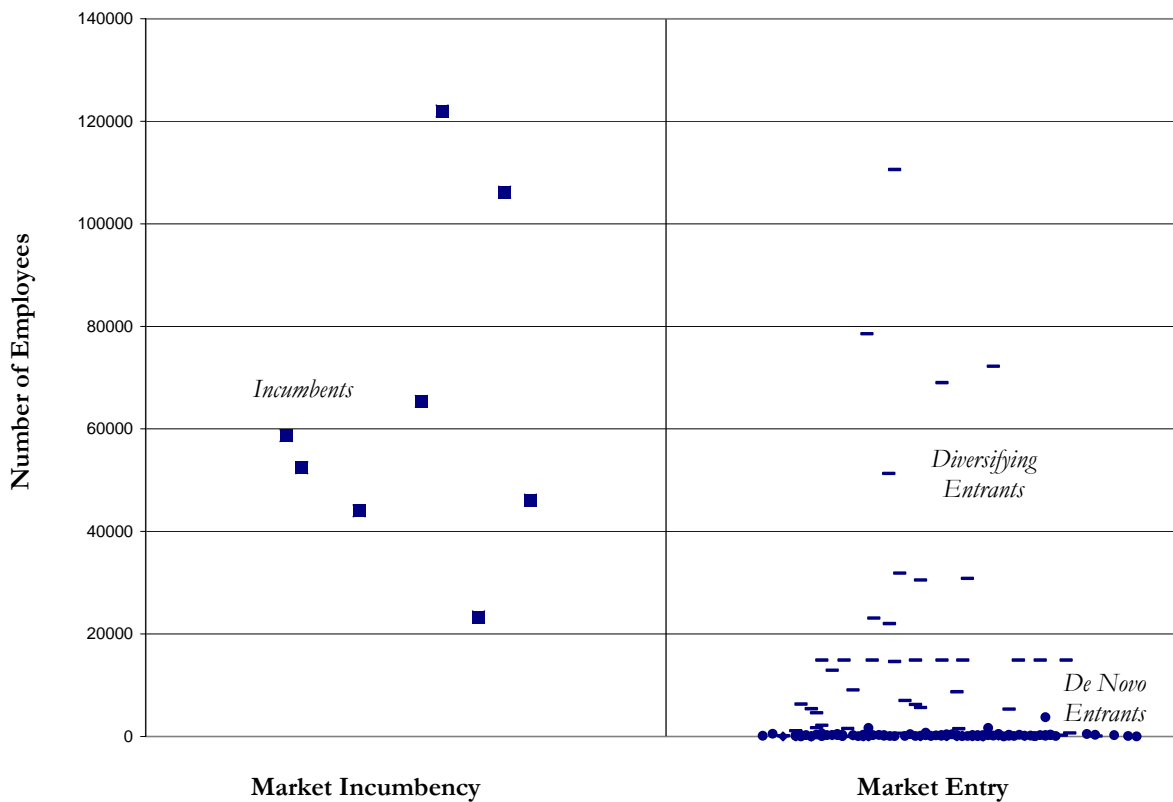
I start by presenting Figures 5.1 and 5.2, which display the size and age distribution by firm category for the final sample, respectively. The x-axis for both graphs represents a binary variable for market incumbency vs. market entry. I “disperse” the data points horizontally within each of these two categories for visual clarity only. Instead of marking organizational experience per se in the graph, I use three different markers to distinguish among the three populations of firms directly.

Note the presence of all three firm categories in the distributions shown in figures 5.1 and 5.2, confirming the appropriate fit of this sample for the current study. More importantly, observe the similarity both in size and in age of diversifying entrants to the other two categories of firms at either end of the spectrum. This characteristic is informative both for the use of firm size and age as control variables in analyses in the present study, and more broadly, for studies of innovation linked to either variable.



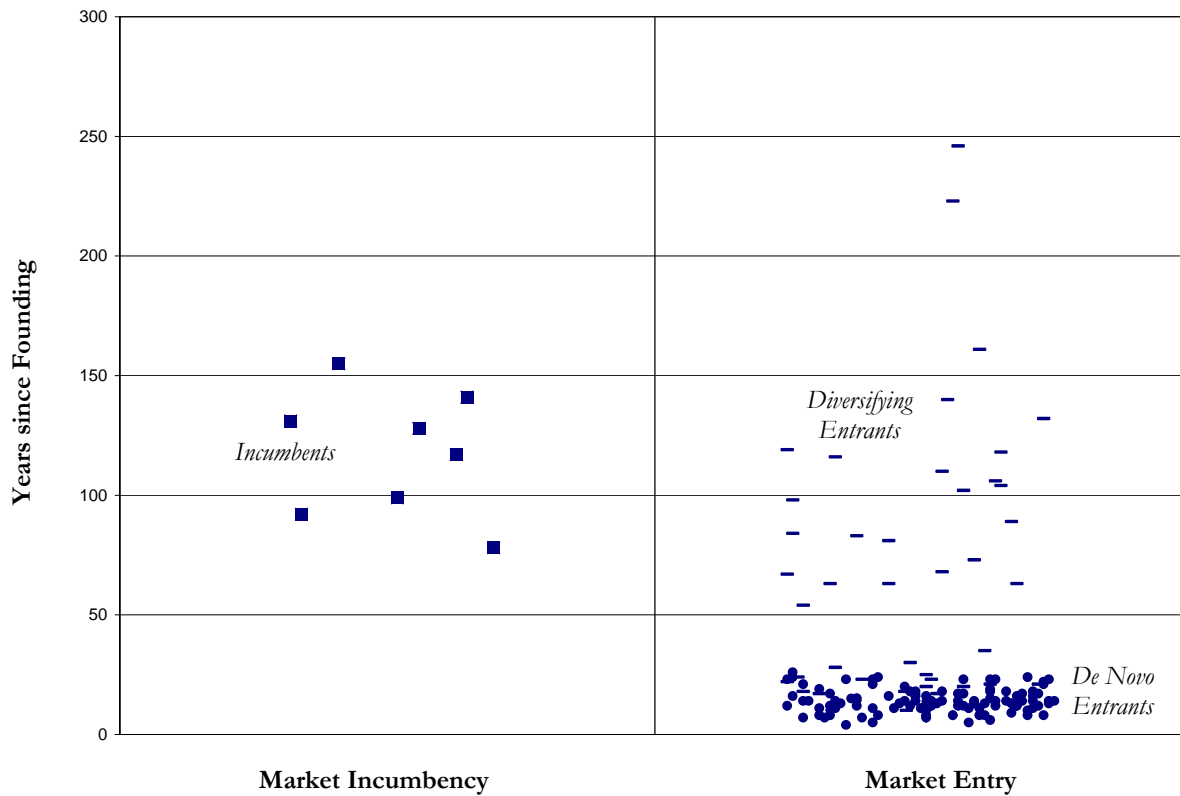
**FIGURE 5.1**  
**Distribution of Firms Competing in Targeted Anti-Cancer Drugs**  
**by Firm Category and Size**

(■ incumbent, — diversifying entrant, ● de novo entrant)



**FIGURE 5.2**  
**Distribution of Firms Competing in Targeted Anti-Cancer Drugs**  
**by Firm Category and Age**

(■ incumbent, — diversifying entrant, ● de novo entrant)



On the one hand, studies of innovation and firm size clearly aim at understanding Schumpeterian dynamics, the dynamics of incumbents vs. entrants, and such studies have been characterized by persistently inconsistent results (see Acs and Audretsch [1990] for a review). A look back at Figure 5.1 can shed light on this issue. Firm size does not perfectly correlate with market incumbency in the market for anti-cancer drugs, and possibly, in many other markets. To the extent that the Schumpeterian dynamics these studies are trying to understand are focused on

incumbents' empirical regularities, firm size will constitute an incomplete approach, with significant measurement error in empirics, and significant concerns in construct validity in theoretical considerations. In fact, in the 165-firm sample in this study, the correlation index between firm size and incumbency is 0.62 (significant at the  $p < 0.00001$  level). When I create a binary variable for "established firms" (including both incumbents and diversifying firms), the correlation index between that variable and firm size is still large and significant with a value of 0.54 (still significant at the  $p < 0.0001$  level). Firm size might or might not be a good proxy for market incumbency and the correlation value will vary across markets depending on whether the market structure supports the formation of more or fewer de novo firms. For the purposes of the present study, I will present statistical models with and without firm size included, since including both incumbency and firm size will produce multicollinearity.

The relationship between market incumbency and firm age is less clear. The variables are, again, significantly correlated. In the 165-firm sample in this study, the correlation index between market incumbency and firm age is 0.45 ( $p < 0.0001$ ), and between "established" and firm age is 0.67 ( $p < 0.0001$ ). Although I treat the high correlation as an indicator of possible multicollinearity and therefore run models with and without firm age, it is unclear whether there are theoretical implications. Research on age (e.g., Stinchcombe, 1965; Freeman, Carroll and Hannan, 1983; Sørensen and Stuart, 2000) is in fact about *aging* (continuously time-varying covariates) and not about *differences in age* (cross-sectional) as I implement here. Furthermore, in his original work, Stinchcombe (1965) stated that a combination of economic and technical conditions would explain cases contradicting his theory. In

his specific example of the deviant case of the water transportation industry, Stinchcombe (1965) wrote that “clearly, the introduction of the steamship, diesel propulsion, and the steel hull reorganized the shipbuilding and water-transportation industries much more than I had anticipated” (p. 156). This assertion implies that his classic theory addresses “stable” markets, that is, it is not immediately applicable to the study of the transition of a market from its state under an old technology to its state under a new one. Outside of the original theory, it is difficult to relate Schumpeterian dynamics to classic empirical tests of firm aging (e.g., Carroll and Delacroix, 1982; Freeman, Carroll and Hannan, 1983). Such classics refer to market entry, and the discussion of advancement in the R&D process (the objective of this study, and the connection to the classic work of Henderson [1993] that motivated the analysis) represents rather the *threat* of entry and not market entry per se (Tirole, 1988).<sup>50</sup> The only study linking aging dynamics with R&D competence (i.e., innovative capacity) is Sørensen and Stuart (2000). As is more clearly seen in these authors’ biotechnology sub-sample, the firms under study are a single population of de novo firms,<sup>51</sup> precisely the only population that is not under transition, neither between technologies (incumbents) nor between markets (diversifying entrants). That is, the population of de novo firms included in their analysis has no market incumbency and no prior organizational experience.

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<sup>50</sup> That is, mine is not a study of firms launching products in a market (i.e., market entry), but rather of firms advancing product candidates through their R&D process and thereby increasing their probability of soon having a product to launch into the market (i.e., threat of entry).

<sup>51</sup> Since the study in Sørensen and Stuart (2000) was not about creative destruction (i.e., about incumbent failure), the authors do not present the firm profiles. I infer the profile of their firms from their statement that “because the biotechnology sample consists of dedicated producers only, the age clock for the firms in this sample always begins at incorporation” (p. 93). The inference is, however, further complicated by the fact that the study, as other research in firm age, is at the industry- and not market-level of analysis, since many of the aging processes hold equally at the industry and market levels (e.g., legitimacy of the organizational form of the firm within its environment).

Former work has discussed how changes in a firm's environment can generate a change in the organization equivalent to a partial resetting of its age (Amburguey, Kelly and Barnett, 1993). This implies that as an organization continues to operate, its chronological age reflects progressively less the true measure of the firm's competence (perhaps better reflected in a measure of organizational experience that could be made continuous and market- and technology-specific). Future research will be needed to clarify the underlying theoretical connection between the transition of established firms and the general process of firm aging.<sup>52</sup> For the present study, I will only consider the high correlation of market incumbency and firm age (as cross-sectional differences) when attempting to avoid multicollinearity in statistical analysis.

## **5.2 Competence in Preclinical and Clinical Drug Development**

I now move to the analysis of the 2,281-drug sample to measure differences in the competences in preclinical drug design and clinical trial execution jointly. I proceed to the analysis of the 113-drug sample to measure preclinical drug design isolated afterwards, in section 5.3.

Figures 5.3a and 5.3b offer a qualitative overview (prior to controls) of the differences in these competences measured jointly. The figure shows the cumulative risk of approval generated through the Cox Model Analysis. That is, the vertical axis represents higher risk of getting an approval, and of getting it faster. For clarity, the

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<sup>52</sup> In my opinion, the process of experience accumulation is a process of aging. Firm age, however, becomes an inaccurate proxy for established firms (although appropriate for de novo firms). This is because each organizational change that the established firm faces partially resets its clock. Therefore, as the firm accumulates experience, its "chronological" and its "organizational" clocks differ progressively more. Using a firm's chronological age then seems inaccurate, although using binary variables (incumbent vs. entrant, and established vs. de novo) is as well an extremely crude estimation of the phenomenon.

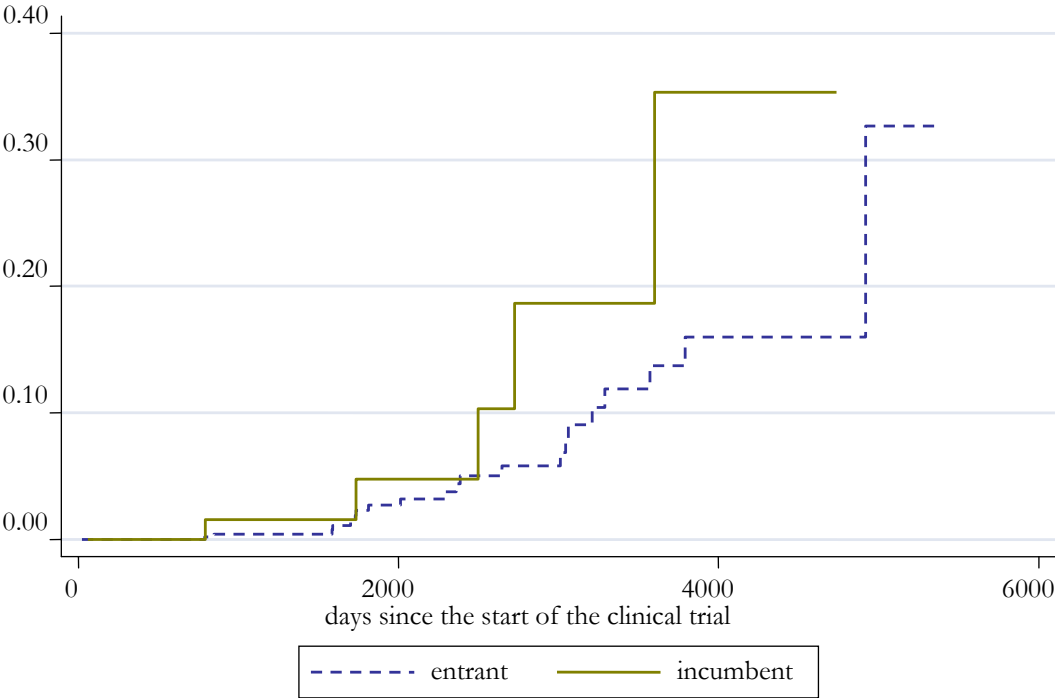
sample for this figure is stratified on targeted anti-cancer drugs only, so as to measure differences in competence in the R&D of the new technology only.

The main finding in the event history analysis can be seen in the contrast between Figures 5.3a and 5.3b: the performance of incumbents vs. entrants looks drastically different unless the latter are separated into “experienced” vs. “inexperienced” (i.e., diversifying vs. de novo) entrants. When separated, diversifying entrants’ performance seems similar to that of incumbents. Actually, it is established (i.e., incumbents and diversifying entrants) vs. de novo firms that are the most relevant categories for comparative analysis for the overall picture of the R&D process under disruption.

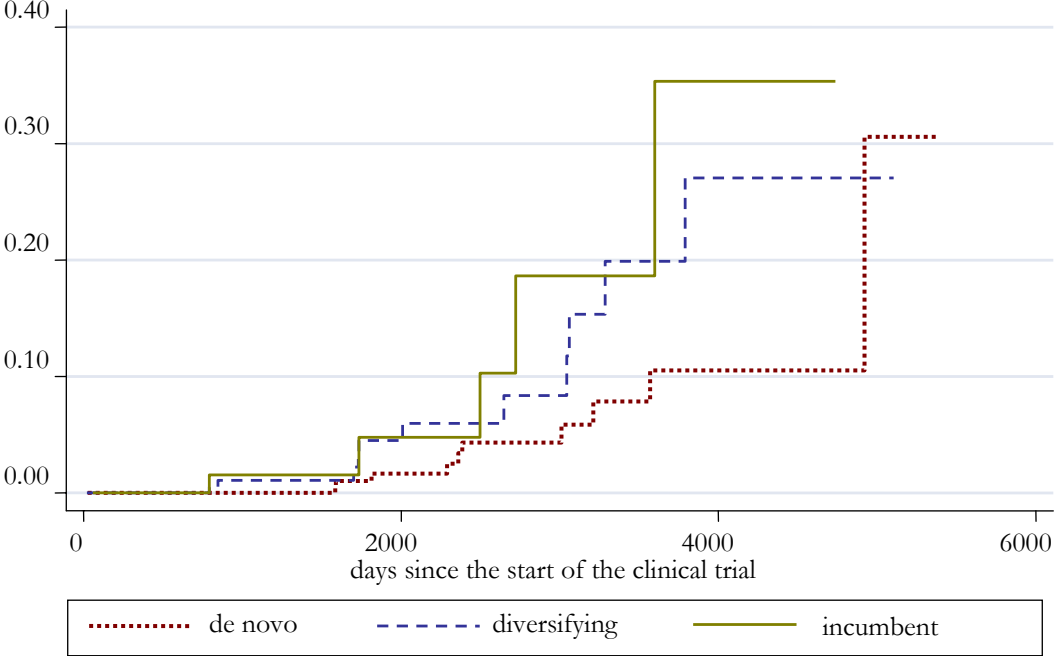
Moreover, notice the direction of competitive advantage: when both preclinical and clinical (i.e., most and least disrupted) R&D sub-categories are taken into account, and entrants are disaggregated, both populations of established firms outperform de novo entrants. This implies that in this setting and for the overall picture of R&D, competence re-use, the advantage stemming from organizational experience, overrides organizational inertia, the disadvantage.

**FIGURE 5.3**  
**Cumulative Hazard (Nelson-Aalen) Graphs**  
**Event modeled: Drug Approval *among Targeted Anti-Cancer Drugs Only***  
**(Spells = 991, events = 22)**

**(5.3a) Comparison of incumbents vs. entrants**



**(5.3b) Comparison of incumbents, diversifying and de novo entrants**



I present now the corresponding quantitative analysis. Table 5.1 offers descriptive statistics. Table 5.2 shows results on the event history analysis (Cox model) for the entire sample, whereas Table 5.3 is stratified on targeted drugs.

**TABLE 5.1**  
**Preclinical Drug Design and Clinical Trial Execution,**  
**Descriptive Statistics and Correlation Matrix**  
**(N = 2,281)**

	Count	Mean	Std.Dev.	Min.	Max.
(1) Incumbent	499				
(2) Diversifying	864				
(3) Targeted	991				
(4) Firm Age		69.8	65.7	4	246
(5) Firm Size		30,200	39,937	10	122,000
(6) Cumulative		405	250	1	918
(7) Drug Novelty		27.6	40.6	1	222
(8) R&D Alliance	44				

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
(1) Incumbent	1							
(2) Diversifying	-0.41	1						
(3) Targeted	-0.11	-0.039	1					
(4) Firm Age	0.44	0.31	-0.14	1				
(5) Firm Size	0.64	0.07	-0.12	0.80	1			
(6) Cumulative	-0.32	0.09	0.23	-0.24	-0.26	1		
(7) Drug Novelty	-0.007	-0.02	0.002	-0.02	-0.02	-0.28	1	
(8) R&D Alliance	-0.028	-0.05	-0.02	-0.05	-0.04	-0.08	0.03	1



**TABLE 5.2**  
**Preclinical Drug Design and Clinical Trial Execution,**  
**Cox Model Analysis of Drug Approval**  
**(2,281 Spells, 55 Events)**  
All Coefficients in *Hazard Rates*

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>	<b>Model 4</b>
Incumbent	2.4* (0.87)	2.71* (1.13)	3.2** (1.35)	5.39** (3.70)
Diversifying		1.21 (0.54)	1.39 (0.61)	1.82 (0.88)
Targeted	1.01 (0.32)	0.61 (0.29)	0.67 (0.33)	0.67 (0.33)
Incumbent x Targeted	0.79 (0.51)	1.31 (0.99)	1.01 (0.77)	0.95 (0.74)
Diversifying x Targeted		3.02+ (2.00)	2.87~ (1.95)	2.70~ (1.83)
Firm Age				0.99 (0.00)
Firm Size				0.99 (0.00)
Cumulative Introduction			0.99 (0.001)	0.99 (0.00)
Drug Novelty			1.38*** (0.12)	1.36*** (0.12)
R&D Alliance			2.17~ (1.14)	2.06~ (1.11)
<b>Log Likelihood</b>	<b>-315</b>	<b>-311</b>	<b>-305</b>	<b>-304</b>

~ marginal, +  $p < 0.1$ , \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$  Standard errors in parentheses.

**TABLE 5.3**  
**Preclinical Drug Design and Clinical Trial Execution,**  
**Cox Model Analysis of Drug Approval**  
*Only Targeted Drugs*  
**(991 Spells, 22 Events)**  
All Coefficients in *Hazard Rates*

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>	<b>Model 4</b>
Incumbent	1.99 (1.12)	3.72* (2.36)	3.45* (2.15)	4.06* (3.47)
Diversifying		3.75** (1.78)	3.53* (1.79)	4.24** (2.37)
Firm Age				0.99 (0.00)
Firm Size				1.00 (0.00)
Cumulative Introduction			1.00 (0.00)	1.00 (0.00)
Drug Novelty			1.32* (0.16)	1.29* (0.16)
R&D Alliance			1.64 (1.72)	1.54 (1.67)
<b>Log Likelihood</b>	<b>-110</b>	<b>-106</b>	<b>-104.4</b>	<b>-104.1</b>

~ p < 0.15, + p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

The first point to observe is that, even during this period of transition when both old and new technologies compete, incumbents remain the best at researching the old technology. This is reflected in all models in Table 5.2 where the variable “incumbent” is significant and greater than 1, after controlling for the effect of “targeted,” the interaction of both variables, and the rest of the controls. Incumbents were the leaders of the cytotoxic anti-cancer drug development regime (i.e., the old technology regime) and retain their advantage as that technology dies, even though both populations of entrants invest in cytotoxic anti-cancer drug development in parallel to their entry into targeted anti-cancer drugs.

The dynamics shown in Figure 5.3 can be seen quantitatively more clearly in Table 5.3 where models are stratified on targeted drugs only. In all models in Table 5.3, the competence to do preclinical and clinical research in the new technology, targeted anti-cancer drugs, for incumbents and diversifying entrants is significantly higher than that for de novo firms. But this difference would not be apparent under the traditional analysis of incumbents vs. entrants. To see this, notice that Model 1 is not significant, whereas Models 2, 3 and 4 (that include controls, with and without firm age and size in the equation) all exhibit a significant and larger than 1 hazard rate for incumbents and diversifying entrants. In fact, a test for differences in the coefficients for incumbents and diversifying entrants in Models 2, 3 and 4 are all not significant. That implies that, when the overall picture of competition in R&D is taken into account, with both destroyed and re-usable competences included, the two categories with most distant outcomes between them are not incumbents vs. entrants, but established vs. de novo firms.

Lastly, “Drug Novelty” is significant as expected but does not alter the results. More importantly, at least in Table 5.2 where the sample size is larger, the variable “R&D Alliance” is almost significant in both Models 3 and 4 ( $p < 0.14$  and  $p < 0.17$ , respectively). These results follow the direction of prior research that focuses on the impact of research alliances in the innovative ability of firms in biotechnology (e.g., Powell, Koput and Smith-Doerr, 1996).

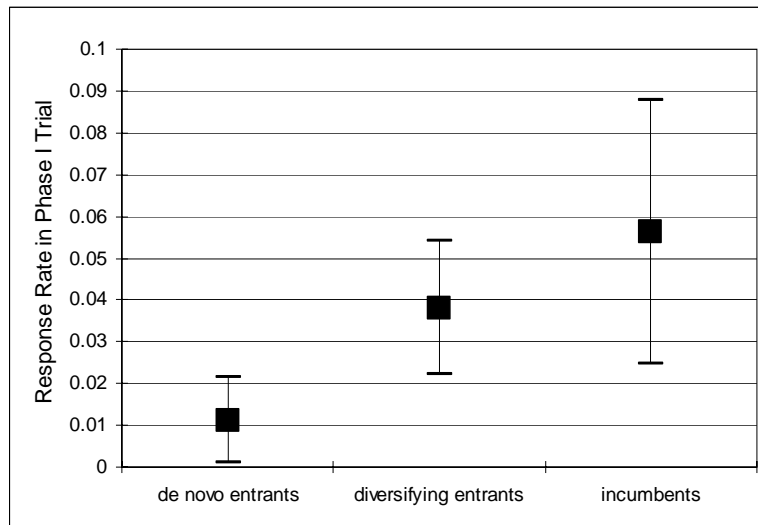
### **5.3 Competence in Preclinical Drug Design**

I advance now to the analysis of the differences in competence in preclinical drug design alone. This then isolates within the R&D process, the one area where

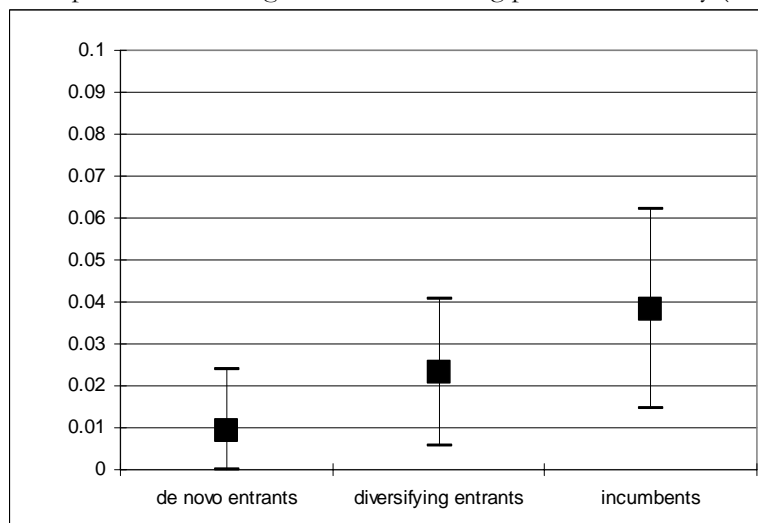
competences are fully destroyed for incumbents. A qualitative overview (prior to controls) for the measurement of competence in preclinical drug design is offered in Figure 5.4. This figure shows mean values on response rate and 95% confidence intervals (all prior to controls).

**FIGURE 5.4**  
**Differences in Means in Competence in Preclinical Drug Design** (95% CI)

**(14a).** Mean response rates of *all*, cytotoxic and targeted anti-cancer drug phase I trials (N = 172 trials).



**(14b).** Mean response rates of *targeted* anti-cancer drug phase I trials only (N = 58 trials).



Descriptive statistics are provided in Table 5.4. Regression analyses are less straightforward because the dependent variable, response rate, is a proportion and is therefore bounded between 0 and 1. I therefore first analyze the data with censoring through a Tobit Model with fixed upper and lower bounds (Maddala, 1983). This analysis is presented in Table 5.5 for the full sample and in Table 5.6 for the sub-sample stratified on targeted anti-cancer drugs. I then repeat the analysis of the stratified sample of targeted drugs only in two more specifications. The first one is reported in Table 5.7 and consists of an unbounded Generalized Linear Model also reported in the econometrics literature as appropriate for regressing proportions (Papke and Wooldridge, 1996). The second is reported in Table 5.8 and is a basic Ordinary Least Squares (OLS) Model. All analyses support basically the same conclusions.

**TABLE 5.4**  
**Preclinical Drug Design, Descriptive Statistics and Correlation Matrix**  
**(N = 172 Trials)**

	Count	Mean	StdDev	(1)	(2)	(3)	(4)	(5)	(6)
(1) Response Rate		3.5%	7.7%	1					
(2) Incumbent	49			0.17	1				
(3) Diversifying	73			0.03	-0.54	1			
(4) Two or fewer Tumor Types	36			0.17	-0.03	-0.03	1		
(5) Targeted	58			-0.12	0.01	-0.18	0.20	1	
(6) Death Rate		0.5%	1.7%	0.08	0.19	-0.001	-0.04	-0.11	1

**TABLE 5.5**  
**Preclinical Drug Design**  
**Tobit Analysis of Response Rate during Phase I Trial**  
**(N = 172)**

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>	<b>Model 4</b>
Constant	-0.05** (0.02)	-0.13** (0.04)	-0.14*** (0.04)	-0.14*** (0.04)
Incumbent	0.05+ (0.03)	0.13** (0.05)	0.13** (0.04)	0.13** (0.04)
Diversifying		0.10* (0.04)	0.10* (0.04)	0.10* (0.04)
Targeted	-0.06+ (0.03)	-0.06 (0.06)	-0.08 (0.06)	-0.08 (0.06)
Incumbent x Targeted	0.04 (0.06)	0.03 (0.08)	0.03 (0.08)	0.03 (0.08)
Diversifying x Targeted		0.02 (0.08)	0.01 (0.07)	0.02 (0.07)
Two or fewer Tumor Types			0.09** (0.03)	0.09** (0.03)
Death Rate			-0.09 (0.8)	-0.08 (0.8)
Death Rate x Targeted			2.24 (1.56)	2.26 (1.57)
Replicate Trial				0.01 (0.02)
Log likelihood	-27	-22	-17.2	-17.1

+ p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

**TABLE 5.6**  
**Preclinical Drug Design**  
**Tobit Analysis of Response Rate during Phase I Trial**  
*Only Targeted Drugs*  
**(N = 58)**

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>	<b>Model 4</b>
Constant	-0.06* (0.02)	-0.10** (0.04)	-0.10** (0.03)	-0.10** (0.03)
Incumbent	0.07* (0.03)	0.11** (0.04)	0.09* (0.03)	0.09* (0.03)
Diversifying		0.08+ (0.04)	0.06+ (0.03)	0.06+ (0.03)
Two or fewer Tumor Types			0.05+ (0.02)	0.05+ (0.02)
Death Rate			1.70* (0.7)	1.70* (0.7)
Replicate Trial				-0.01 (0.02)
Log likelihood	-1.8	0.5	4.4	4.5

+ p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

**TABLE 5.7**  
**Preclinical Drug Design**  
**GLM Analysis of Response Rate during Phase I Trial**  
*Only Targeted Drugs*  
**(N = 58)**

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>	<b>Model 4</b>	<b>Model 5</b>
Constant	-4.18*** (0.36)	-4.68*** (0.78)	-5.25*** (0.70)	-5.12*** (0.75)	-5.25*** (0.70)
Incumbent	0.96* (0.47)	1.46+ (0.83)	1.43+ (0.78)	1.46* (0.75)	1.43+ (0.80)
Diversifying		0.94 (0.86)	0.91 (0.83)	0.86 (0.85)	0.91 (0.83)
Two or fewer Tumor Types			1.11** (0.42)	1.09** (0.40)	1.11** (0.44)
Death Rate			20.35*** (3.12)	18.92*** (3.12)	20.35*** (3.16)
Replicate Trial				-0.34 (0.47)	
Clustered Standard Errors					✓
Log pseudo-likelihood	-4.8	-4.7	-4.45	-4.44	-4.45

+ p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

**TABLE 5.8**  
**Preclinical Drug Design**  
**OLS Analysis of Response Rate during Phase I Trial**  
*Only Targeted Drugs*  
**(N = 58)**

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>
Constant	0.01** (0.005)	0.00 (0.00)	0.00 (0.00)
Incumbent	0.02+ (0.01)	0.02* (0.01)	0.02* (0.01)
Diversifying		0.01 (0.01)	0.01 (0.01)
Two or fewer Tumor Types			0.02+ (0.01)
Death Rate			1.30*** (0.09)
R <sup>2</sup>	0.07	0.09	0.36

+ p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

First notice the performance of incumbents at researching the old technology. This can be seen in table 5.5 in the size and significance of the coefficient for “incumbent” in all models. Although the coefficient is in the right direction in Models 2 and 3, appearing larger for incumbents than for diversifying entrants, the test for differences in the coefficients is not supported ( $p < 0.3$  in all models), possibly as a consequence of the small sample size.

Furthermore, notice the unexpected result that incumbents are at no disadvantage vs. entrants (aggregated or not) in the most disrupted area of R&D, as indicated by all interaction terms in Table 5.5 being no different from zero. In fact, all established firms (whether incumbents or diversifying entrants) are again at an advantage vs. de novo firms in this sub-category of the R&D process as seen when the sample is stratified on targeted drugs only (to gain power). The main effects for incumbents and diversifying entrants are significant in Table 5.6 for all models. In all cases, controlling for the number of tumor types is significant as expected, but does not change the direction or significance of coefficients, neither does controlling for the death rate (although this variable and its interaction with “targeted” drastically improves the proportion of variance explained by the models). Lastly, controlling for the presence of trials sharing the same drug (refer to Figure 4.7) does not change any of the above results. This can be seen in the inclusion of the binary variable “Replicate Trial” in Model 4 in Table 5.5 (full sample) and Model 4 in Table 5.6 (sample stratified for targeted drugs only) for the Tobit specification. It is also present in Table 5.7 for the Generalized Linear Model specification, through the inclusion of the same binary variable in Model 4, and the analysis with standard errors clustered around trials sharing the same drug shown in Model 5.



## 5.4 Discussion

In previous chapters, I presented the theoretical motivations for the present study. I followed the “chain of causality” (Porter, 1991) reported in the literature for the market underperformance of market incumbents during a period of technological change. After finding research incompetence as one of its roots, I then followed the root of that incompetence to organizational inertia. Finally, I followed the root of that inertia, and found prior organizational experience. I argued that if we were to explain incumbents’ incompetence in researching a new technology by the presence of organizational inertia stemming from these firms’ prior organizational experience, we would have to be willing to assume that all competent entrants are devoid of organizational inertia, that is, are de novo firms. This latter assumption, though, contradicted empirical evidence. I therefore called for the need to decouple market incumbency from organizational experience in studies of R&D competition during periods of technological change. Although the focus within creative destruction is on the fate of market incumbents, the underlying dynamics of organizational inertia are connected to organizational experience, and hence to all established firms in competition (incumbents and diversifying entrants). I therefore implemented three categories of firms to empirically decouple what at this point are two binary variables: incumbency and experience, and therefore for the first time distinguished between incumbents and established firms.

I explained how this decoupling to appropriately assign the disadvantage of organizational inertia required the finer measurement of variance in competence destruction to appropriately assign the advantage of competence re-use to all established firms in competition.

Certainly, the analyses presented in this chapter show that when performing the analysis on the overall R&D process (with destroyed and re-usable competences), the traditional analysis and that I propose generate different conclusions. When the comparison of incumbents vs. entrants is substituted with the three separate categories of incumbents, diversifying and de novo firms, the last category is the one that appears distinguishably apart. In fact, the statistical analysis supports the clear distinction not between incumbents and entrants, but between established and de novo firms. This then matches our underlying theory more appropriately. When all competences are considered, destroyed and re-usable, incumbents and diversifying entrants share mechanisms that de novo firms do not undergo. These underlying mechanisms should set incumbents and diversifying entrants apart under a larger umbrella as established firms, since they are the only two firm categories that engage in inertia and competence re-use, even though the level of inertia and type of competences to re-use are not precisely the same, neither between nor within these two firm categories.

Furthermore, the reversed direction of performance in the analysis of overall R&D in this study (i.e., preclinical and clinical jointly) is informative as well. It implies that the advantage of competence re-use available from prior organizational experience (whether it is experience in other markets in the case of diversifying entrants, or of undisrupted competences in the focal market for incumbents) outweighed the disadvantage of organizational inertia among established firms. Expert interviewees confirmed these dynamics: although organizational inertia is a relevant impediment to innovation among established firms, in this setting these

firms have found ways to compensate for it, finding as the next hurdle the need to appropriately re-use and newly develop required competences.

Beyond the answer to my original research question, the analysis of the subsequent preclinical drug design competence offered the opportunity to engage in a theory-building exercise to generate additional insight into the dynamics of creative destruction. In an area of R&D where competences are described as fully destroyed for incumbents, these firms outperform all other firms. Indeed, the least competent category of firms appears to be de novo entrants.

Neither organizational inertia nor competence re-use explains why incumbents outperform de novo entrants and match diversifying entrants (even outperform them, in alternative specifications) in this particular area. Compensating for their organizational inertia would only make them equally competent to de novo firms and underperforming diversifying entrants. Incumbents must have some additional competence to re-use.<sup>53</sup> This point highlights a crucial assumption in current studies of creative destruction that requires revision. Based on the present study, I generate a new proposition: R&D competences can be decomposed into a technology-specific side (e.g., mechanism-driven drug design used to perform preclinical design of targeted anti-cancer drugs) and an application-specific side (e.g.,

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<sup>53</sup> Alternatively, incumbents could be accruing new competences at an advantaged rate over that of diversifying entrants and de novo firms. I have, at this point, no reason to believe that any mechanism would support this alternative. In fact, my original hypothesis was that de novo firms would have a faster rate of new competence development, precisely because they might attract personnel with different characteristics (e.g., more qualified scientists). In an attempt to control for such differences, I searched *The Complete Marquis Who's Who* database for information on the qualifications of personnel working at each firm in the sample. Although significantly limited, the information did not suggest that the assignment of personnel was biased in terms of their qualifications across populations of firms. Furthermore, in interviews I came across ex-employees of “big pharma” established firms working now with a de novo firm, as often as recent graduates from prestigious universities working with an established firm. Future research is necessary to substantiate differences in the rate of new competence development across firm categories.

competence in the research of cancer as a disease). Under the current assumption in the creative destruction literature that the technological platform (i.e., technology-specific side of R&D competence) is the only source of competitive advantage in R&D, once the existing technological platform for some area is destroyed by a radical technological change, incumbent firms are left at a serious disadvantage in that area. However, if there is an application-specific side of R&D competences, this has, by the start of the disruption, accrued only to incumbents. This side of R&D competences might represent a unique source of competitive advantage for incumbents even in areas of R&D where the technology-specific R&D competences are destroyed.

The proposition of decomposing the R&D competences required for competition in a given market under a given technological regime is not at odds with prior literature. Consider the proposition that the full domain of an organization can effectively be decomposed into three elements: technology, product and clientele as offered by Haveman (1992) in a study of diversification in the Savings and Loan Industry in California.<sup>54</sup> Once the commercialization stage, that is, the clientele, is left out of the scope of the project, as is the case in my present study, the remaining portion of the organizational domain matches the R&D process for a high-technology organization. The R&D process then corresponds to the two remaining elements of the organizational domain: technology and product (i.e., what I refer to as application). Incumbents are familiar with the “product” whereas diversifying entrants are familiar with the “technology.” The incursion into the new technology

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<sup>54</sup> Haveman (1992) advanced the previous characterization of an organizational domain as market and technology (Roberts and Berry, 1985). In Haveman’s setting, however, only diversifying entrants are present in the newly born markets under study (no incumbents by definition but also no de novo firms), probably as a consequence of the specific market structure and environmental change.

to develop products for the focal market represents, therefore, related diversification for all established firms, both incumbents and diversifying entrants, at least a priori (as the disruption unfolds, firms might realize that some were “more related” than others).

Another way of saying this is to go back to Wernerfelt’s (1984) original proposition of conceptualizing the operation of established firms in a matrix of product markets vs. resource bases (see Figure 5.5 for an illustration adapted from the original).

**FIGURE 5.5**  
**The Product Markets vs. Resource Bases Matrix**  
 (adapted from Wernerfelt, 1984)

	<i>Market 1</i>	<i>Market 2</i>	<i>...</i>	<i>Market n</i>
<i>Resource 1</i>				
<i>Resource 2</i>				
<i>...</i>				
<i>Resource m</i>				

Common practice in the Strategy field (resource-based view in particular) has been to center on resource bases (including among them technological platforms) that are (re)usable for more than one market, so as to match symmetrically the fact that a market requires the use of several resource bases. However, there is a possibility that some resource bases (e.g., some parts of R&D competences) are application-specific and hence that they both survive shocks of technological competence destruction and are a unique source of competitive advantage for market incumbents.

Distinguishing between the technology and the application begins to reunite what has been criticized as too many disconnected definitions within the literature on technology management (Gatignon, et al., 2002; Chesbrough, 2001, p.18). The characterization of technological change that Henderson and Clark (1990) originally proposed (as incremental, modular, architectural or radical) concerns purely the technology-specific side. Since the application remains undisrupted, if there are any competences specific to the application, they should have accrued only to incumbents and should represent a source of competitive advantage only to them (how valuable this source of competitive advantage is constitutes a different question). Alternatively, when it is the application itself that is disrupted, in terms of the dimensions of merit that the product itself should contain for consumers to pay further price premiums, we utilize the terminology put forth by Christensen (1997): sustaining vs. disruptive innovation. In the case of disruptive innovation, the application will be altered and any application-specific competences destroyed for incumbents.

The four waves of disruption in the market for photolithographic aligners included in Henderson (1993) represent architectural innovations in terms of the firms' technological competences. The application, however, remains undisrupted in terms of dimensions of merit and is hence a sustaining innovation (see Henderson, 1995). In the case I analyze in the present study on the market for anti-cancer drugs, the innovation is radical in terms of the technological side, but again sustaining in terms of the application. To see this, refer to Table 5.8.

**TABLE 5.8**  
**Trends in Efficacy of Anti-Cancer Drugs as Estimated by Mortality Rates and**  
**5-Year Survival Rates for Main Cancer Indications**

Type of Cancer	Estimated new cases 2000 <sup>1</sup> (000's)	Mortality Rate 1973 <sup>2</sup>	Mortality Rate 1995 <sup>2</sup>	Δ in Mortality Rate	5-year Survival Rate 1974-1979 <sup>2</sup>	5-year Survival Rate 1989-1994 <sup>2</sup>	Δ in 5-year Survival Rate
All Sites	1.22MM	–	–	–	–	–	–
Breast (Female)	183	26.9	25.2	-1.7	74.5	85.3	10.8
Prostate	180	21.7	24.9	3.2	68.7	93.4	24.7
Lung/bronchus	164	34.8	49.3	14.5	2.4	14.1	11.7
Colon/rectum	130	21.9	17.4	-4.5	49.5	62.1	12.6
Non-Hodgkins Lymphoma	55	4.7	6.9	2.2	47.1	51.4	4.3
Bladder	53	–	–	–	–	81	–
Melanoma	48	–	–	–	–	88	–
Uterus	36	–	–	–	–	84	–
Oral Cavity	30	–	–	–	–	53	–
Pancreas	30	8.6	8.3	-0.3	2.5	3.9	1.4
Kidney	29	–	–	–	–	60	–
Leukemias	27	6.7	6.3	-0.4	34.3	42.8	8.5
Ovary	23	8.4	7.7	-0.7	36.8	49.9	13.1
Brain/Nervous System	–	3.7	4.1	0.4	22.4	30.3	7.9
Stomach	–	7	4.2	-2.8	15.3	20.8	5.5

- SOURCES: 1 American Cancer Society, 2000, *Cancer Facts & Figures* as quoted in SG Cowen Securities Corporation, 2000, "US top 13 types of cancer ranked by forecast number of new cases in 2000, with percent growth in incidence for each type of cancer in the period 1992 to 1997, and five-year survival rate in percent for each type of cancer in the period 1989 to 1995" *PHARMACEUTICAL THERAPEUTIC CATEGORIES OUTLOOK*, Part 28.
- 2 American Cancer Society, 1996, 1997 and 1998, *Cancer Facts & Figures*; New York Times, May 26, 1998, as quoted in Dorlands Directories, 1999, "US top 10 types of cancer ranked by number of deaths in 1998, with percent mortality rates in 1973 and 1995, and for the period 1974 to 1979, and percent survival rate for the period 1989 to 1994," *Cancer Therapy and Related--Cancer Epidemiology Background, Medical & Healthcare Marketplace Guide: 1-409*.

NOTES: "–" indicates information not available.

In Table 5.8 it becomes readily apparent that the market is far from satiated (i.e., far from saturated on a dimension of merit) on the levels of efficacy and safety, the main dimensions of merit considered in an anti-cancer drug. In fact, available

patient accounts (e.g., Bazell, 1998) report how patients are willing to undergo deficits in alternative dimensions of merit in order to gain in efficacy.<sup>55</sup>

If we posit that there is an application-specific side of R&D competence separate from the technology-specific side, we can expand the amount of competences that incumbents can re-use during a period of radical technological change. Incumbent firms can re-use their full competences from the areas of R&D left undisrupted, but even in fully disrupted areas of R&D, they can still re-use their application-specific R&D competences.

Within R&D, the question of whether it is the technology- or application-specific side of competences that are harder to acquire and hence constitute a source of competitive advantage is contingent on the market. This conclusion hence mirrors the usual analysis in the corporate diversification literature for the case of the entire organizational domain (Roberts and Berry, 1985),

For example, it is quite feasible that in the state of the market that transitioned from mechanical to electrical typewriters in the early 20<sup>th</sup> century (Utterback, 1994), it was trivial for IBM as a diversifying entrant to catch up with the application-specific R&D competence of building typewriters, but meaningful to re-use its technology-specific R&D competence at electrical automation.<sup>56</sup> Sperry Rand as an incumbent might not have had a strong source of competitive advantage in its unique competence in typewriter development and assembly in that case. For other

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<sup>55</sup> Bazell (1998) recounts a patient undergoing treatment with newly developed *Herceptin*® reporting that she has consistently stopped traveling out of town for periods longer than one week in order to receive weekly transfusions of the drug at her familiar cancer clinic.

<sup>56</sup> Although in 1961 when IBM introduced its famous *Selectric* (the first best-selling electrical typewriter to hit the market although other versions existed as early as 1936), the company had never been involved in typewriter development or manufacture, the company had certainly been using electricity for automation for some time. In fact, the company introduced its first tabulating equipment with electric key punch in 1923. (Source: [http://www-03.ibm.com/ibm/history/history/history\\_intro.html](http://www-03.ibm.com/ibm/history/history/history_intro.html) visited on November 4, 2005.)



markets, however, such as the market for anti-cancer drugs, the challenge of catching up on the application-specific side of the R&D competence might be considerable for all entrants.<sup>57</sup>

In fact, the existence of two sides of R&D competence seems to be supported by the appreciable structure of de novo firms in this market, the only population of firms that usually cannot afford to emphasize the development of both competences. In interviews, two de novo firms with equally successful corporate experiences (12 years since their foundings, over 100 employees each, completed IPOs, similar 2-building installed facilities) reported taking opposite approaches, supporting the idea that both sides of R&D competence exist and are comparably valuable (Barney, 1991) as sources of competitive advantage. The first de novo firm, betting on the innovative nature of its technological platform, had repeatedly changed targeted diseases (including leaving cancer to pursue immunological disorders and even congestive heart failure with an alliance partner). The other,

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<sup>57</sup> I must also highlight that the direction of the comparison of the two sides of R&D competence is contingent not only on the market, but also on the state-of-the-art of R&D in the market at the time the disruption takes place. During the biotechnology disruption to the R&D process for anti-cancer drugs, application-specific R&D competences could be a comparable source of competitive advantage for incumbent firms. However, a prior revolution took place in the same market with different results. This same market, which could be named a market for cancer treatment prior to the emergence of chemotherapy, was being serviced to a large extent by firms that had been producing x-ray and radiotherapy equipment since the turn of the 20<sup>th</sup> century (Lederman, 1981). In the 1940s, the first anti-cancer drug became available (Chabner and Roberts, 2005), and the market was radically disrupted by chemotherapy. The technology-specific R&D competence (chemotherapy) was radically different from the state-of-the-art of radiotherapy, and the new technology represented a significant improvement in treatment efficacy (Zubrod, 1979). Yet, the application-specific knowledge was not as deep as it is nowadays (little was known about cancer and used in the state-of-the-art radiotherapy-based treatment), and therefore, incumbents did not possess a meaningful source of competitive advantage once the technology-specific R&D competence was radically disrupted. In fact, of the 143 firms listed in *Thomson's Register of American Manufacturers* for the year 1949 under the categories "Apparatus: Physicians," "Apparatus: Therapeutic," and "X-Ray Apparatus," a superset of the x-ray therapeutic and radiotherapy equipment manufacturers, none of them were ever listed as an anti-cancer drug manufacturer in the full *Physician's Desk Reference* collection of 1947-2005. Even firms in this superset such as General Electric X-Ray Corporation of Milwaukee, WI, the predecessor of today's General Electric Medical Systems Division, never launched a cytotoxic anti-cancer drug on the market, and after the advent of cancer chemotherapy instead diversified the exploitation of its technology-specific R&D competence into diagnostic equipment markets.

betting on its application-specific R&D competence in anti-cancer drug development, had repeatedly changed technological platforms and left their original technological platform within their laboratory-scale manufacturing process with no intention of ever commercializing such a platform.

In further interviews, it is unclear whether an application-specific side of R&D competence would consist of deeper knowledge of cancer as a disease, of higher absorptive capacity in the knowledge of this disease<sup>58</sup> (Cohen and Levinthal, 1989, 1990), or of a different mechanism such as preemptive patenting due to first-mover advantage (e.g., Fudenberg, et al., 1983). To the extent that a competitive advantage based on the application-specific side of R&D competence exists and is connected to an enduring mechanism (e.g., higher absorptive capacity in that area), it would then constitute a source of “sustained” competitive advantage (Barney, 1991).<sup>59</sup>

The results in the present paper are in line with the most recent evidence in other studies of innovation, such as the groundbreaking study on the biotechnology revolution offered by Zucker, Darby and Brewer (1998). In that study, the authors are interested in the category of “big pharma” firms, which are equivalent to all incumbents and a sub-set of diversifying entrants in my work. The authors find that “big pharma” firms encountered no disadvantage in the adoption of gene sequencing techniques.

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<sup>58</sup> That is, these firms do not know more about cancer but learn faster about it.

<sup>59</sup> As Barney (1991) explains, the term “sustained” does not imply that it will last forever (p. 103). It simply means it will not be competed away through immediate competition. Still, unanticipated changes in the environment in the future could destroy those sources of competitive advantage. In other words, the competitive advantage will be sustained through incremental innovation, although non-incremental technological changes could again destroy it in the future.

## 5.5 Limitations

It is extremely important to reiterate the *prospective* nature of my study. The transition from cytotoxic to targeted anti-cancer drugs is still taking place. Many years from now a *retrospective* study might find that, in the end, de novo entrants were the most successful competitors on all counts. If that were the case, this paper would still be of value as it shows that incumbents were not disadvantaged (and were actually advantaged vs. some firms) at the beginning of the revolution. Only over time, perhaps when some entrant firms catch up in the application-specific side of R&D competence, might the demise of incumbents begin. In the current literature on creative destruction, to my knowledge, few studies have examined the activity of incumbents over time during a period of radical technological change (namely, Cooper and Schendel, 1976; and Christensen, Suarez and Utterback, 1999). The results in these studies are far different from those in the present paper. In the retrospective study offered by Cooper and Schendel (1976), the authors found that incumbents invested early, became disenchanted by the low quality results of the emerging new technology, and stopped investing. Incumbents only returned when it was too late to compete. In the study presented by Christensen et al., (1999), incumbents also missed the window of opportunity to invest in the new technology. In the present paper, incumbents invest early, get good (even advantageously better) results throughout the R&D process, and continue investing in the radically new technology.

I should also emphasize that the tests presented here are comparisons of categories' means, and such a design does not preclude the possibility of an outlier (or set of outliers) emerging from any of the firm categories included. For example,

this study finds no significant advantage accrued to de novo entrants yet, but that does not rule out the possibility that *one* de novo entrant might outperform all categories and represent the toughest competition. The successful cases of Genentech, a de novo entering the market for diabetes treatment in 1976, and of Amgen, a de novo entering the market for treatment of anemia in 1980, illustrate this point.

## 5.6 Conclusions

Of course, major questions remain. Two are, in my opinion, of utmost importance for future research.

On the one hand, an important question points to the process of adaptation of established firms, where the processes will potentially be different for incumbents and diversifying entrants. This is of extreme importance because creative destruction is a process of technological change that has been mainly characterized by change through selection and replacement of the category of incumbents, and yet in this case incumbents adapted. Initial evidence in this direction is present in the literature. Zucker and Darby (1997) report a case study of an established firm moving from random to mechanism-driven drug design within pharmaceuticals. Although the firm in the study is an *industry* incumbent and hence there is no information to infer whether this is a market incumbent or a diversifying entrant, the conclusion that such an established firm adapted to the change through the hiring of new scientific personnel is highly informative. It offers empirical evidence regarding the specific mechanism among those argued for in previous theories of adaptation (March, 1981).

On the other hand, another important question points to the discrepancy between the differing results in Henderson and Clark's (1990) cases in the photolithographic aligner market and the case I present in this study. Incumbents and diversifying entrants in Henderson and Clark's (1990) account had differing outcomes (incumbents were selected out of the market and diversifying entrants took over), whereas in my case, they do not (both categories of established firms outperform de novo entrants). Since the underlying dynamics of organizational inertia and competence re-use apply to all established firms, there must be a reason to believe the mechanisms take place differentially between incumbents and diversifying entrants. This point takes us back to the discussion in sections 3.1 and 3.2, where I highlighted the fact that current theories of adaptation to change would apply equally to all established firms in competition, unless an additional mechanism was present to differentiate the fate of incumbents and diversifying entrants. That additional mechanism could be found in any of the stages defined in Chapter Two (Figure 2.2). In the specific case of Henderson and Clark (1990), it could be that architectural innovations represent a greater challenge in terms of organizational inertia for an established firm than do radical and modular innovations. If this is so, then innovations that are radical in the organizational sense as Henderson (1993) proposed actually exhibit a gradient. Because in the photolithographic aligner market, each wave of innovation was architectural only to incumbents yet radical to diversifying entrants, that would explain the differing outcomes between the two categories of established firms. In the case of the anti-cancer drug market and many others present in the literature, the innovations are radical for all established firms

(whether incumbent or diversifying entrant), and hence there is no reason to believe that there will be a differential in inertia.

Even if the amounts of inertia are different for incumbents and diversifying entrants in the cases in Henderson and Clark (1990) and are not different in my present study, it is possible that other determinants play an important role in the adaptation process. The emphasis placed originally by Hannan and Freeman (1989) on the *timing* of the change (p. 70) is of foremost interest as well. If in fact established firms in the biotechnology revolution are adapting through the hiring of new personnel (Zucker and Darby, 1997), it could be that Henderson and Clark's (1990) photolithographic aligner producers were unable to use the same mechanism because their revolution unraveled in fewer years. In the case of the market for anti-cancer drugs, the biotechnology revolution has been evolving since at least 1983, and 23 years later it is still unfolding. In Henderson and Clark's (1990) study, an incumbent was selected out of the market in less than a decade. According to Henderson (1993), contact aligners began to be substituted by proximity aligners in 1973, and substitution was complete by the late 1970s. The same happened for the change from proximity to stepper technology that unraveled between the late 1970s and the early 1980s.

Much research will be necessary to document the determinants of adaptation, selection and succession in research-intensive markets and beyond in the creative destruction literature. My main proposition in this study is to go back to the original contribution in Henderson (1993), which advanced our understanding of the economic phenomenon of incumbent failure through theories of structural inertia

and organizational change, and to take the examination of that intersection one step further.

## Chapter 6

# The Birth of a Re-Usable Competence

## Analysis of Differences in Competence in Process

### Design

In Chapter Four, I described how the competences to execute the research and development of anti-cancer drugs could be broken down into three sub-categories that varied in level of competence destruction for market incumbents: preclinical drug design, process design, and clinical trial execution (refer to Figure 4.4). I chose then to analyze first only preclinical and clinical competences (refer to Figure 4.5) since they represented extremes in the level of competence destruction. I presented the analysis of those two extreme sub-categories in Chapter Five. In the present chapter I address the analysis of the sub-category I left out before, the competence to design manufacturing processes (i.e., process innovations).

#### **6.1 Differences in Competence in Manufacturing Process Design**

In Chapter Four, I discussed how, unlike preclinical and clinical competences that were fully destroyed and fully re-usable (i.e., enhanced) for incumbents respectively, process design competences were only partially destroyed. Whereas drugs derived in the previous technological regime in the market in question were all cytotoxic small-molecule drugs, the new anti-cancer drugs developed with the



influence of biotechnology are not only targeted instead of cytotoxic, but have also expanded beyond small and into large molecules. That is why the competence destruction for process design is only partial: whereas the processes to manufacture small-molecule targeted anti-cancer drugs are the same as for small-molecule cytotoxic ones, the processes to manufacture large-molecule targeted anti-cancer drugs are radically different (remember there are no large-molecule cytotoxic drugs in existence). I refer to such radically new manufacturing processes as rDNA/fermentation technology since such a term describes the main two components of the new technology: recombinant DNA to alter the characteristics of cells, whether bacterial or mammalian; and fermentation technology to massively harness the products of those genetically engineered cells.

As described also in Chapter Five, I assess differences in competence to design rDNA/fermentation technology processes through a dataset comprising all process patents for the 165 firms in the sample for this market competition. In order to analyze the differences in competence, I analyze the rate of patenting per firm category through a Cox Model following the design used previously in the literature (Sørensen and Stuart, 2000). Table 6.1 offers descriptive statistics and Table 6.2 offers the Cox Model results. The omitted category in this analysis is diversifying entrants, since it is the largest. In contrast, analyses in Chapter Five have de novo firms as the omitted category since in both datasets, that of preclinical competences isolated and that of preclinical and clinical competences jointly, de novo firms are the largest category of trials and drugs, respectively.

**TABLE 6.1**  
**Process Design, Descriptive Statistics and Correlation Matrix**  
**(1,322 Spells, 1,251 Events)**

	Count	Mean	Std.Dev.	Min.	Max.
(1) Incumbent	304				
(2) De Novo	230				
(3) Firm Age		68.8	61.02	7	246
(4) Firm Size		21,518	29,391	14	122,000
(5) Incumbent X Firm Age		27.5	52.5	0	155
(6) Cumulative		298	232	0	807

	(1)	(2)	(3)	(4)	(5)	(6)
(1) Incumbent	1					
(2) De Novo	-0.22	1				
(3) Firm Age	0.47	-0.38	1			
(4) Firm Size	0.67	-0.30	0.64	1		
(5) Incumbent X Firm Age	0.97	-0.22	0.50	0.67	1	
(6) Cumulative	-0.35	-0.36	-0.10	-0.19	-0.34	1

**TABLE 6.2**  
**Process Design Competence**  
**Cox Model Analysis of Patent Application Rate**  
**(1322 Spells, 1251 Events)**  
*All Coefficients in Hazard Rates*

	Model 1	Model 2	Model 3	Model 4	Model 5
Incumbent	1.11* (0.06)	0.87* (0.05)	1.18* (0.09)	0.32*** (0.08)	0.42*** (0.11)
De Novo		0.40*** (0.03)	0.31*** (0.02)	0.29*** (0.06)	0.50*** (0.04)
Firm Age			0.99*** (0.00)	0.99*** (0.00)	0.99*** (0.00)
Firm Size			0.99+ (0.00)	0.99** (0.00)	0.99* (0.00)
Incumbent X Firm Age				1.01*** (0.00)	1.01*** (0.00)
Cumulative					1.00*** (0.00)
Log Likelihood	-7,873	-7,803	-7,777	-7,768	-7,612

+ p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

Notice that manufacturing process design is the only sub-category of R&D where diversifying entrants have an advantage over all other firm categories (since the hazard rates for the other two categories are less than 1 and significant compared to the diversifying entrants' baseline). Since the dataset is built through the collection of all patents related to process design for targeted *large-molecule* drugs only, this analysis implies that diversifying entrants are better at designing this radically new sub-set of processes.

In fact, if diversifying entrants have an advantage at designing specifically the processes for targeted large-molecule drugs, distinguishing for large- vs. small-molecule targeted anti-cancer drugs in the analyses presented in Chapter Five (refer to Table 5.3) could offer further insight. Diversifying entrants might have an advantage at the preclinical and clinical development of targeted large-molecule anti-cancer drugs as well. This is because the source of competitive advantage in process design might also be valuable in preclinical and clinical development, or because as the firms' process design competence increased, the learning-by-doing entailed in such an emerging technology (Pisano, 1996) generated spillover effects in the other two areas. Table 6.3 repeats descriptive statistics for the dataset measuring preclinical and clinical competences jointly originally offered in Table 5.1. Unlike the original Table 5.1 in which I distinguished between cytotoxic vs. targeted anti-cancer drugs only, in Table 6.3, I additionally distinguish between targeted drugs that are small vs. large molecules. I do this by including the dummy variable "Targeted Large Molecule." I then stratify further the sample of targeted anti-cancer drugs used for Cox Model analyses in Chapter Five (Table 5.3 originally) into two separate Cox

Models here: I analyze in Table 6.4 only those that are targeted small-molecule drugs; and in Table 6.5 only those that are targeted large-molecule drugs.

**TABLE 6.3**  
**Preclinical Drug Design and Clinical Trial Execution,**  
**Descriptive Statistics and Correlation Matrix**  
*Only Targeted Drugs*  
**(N = 991)**

	Count	Mean	Std.Dev.	Min.	Max.
(1) Incumbent	162				
(2) Diversifying	354				
(3) Targeted Large Molecule	638				
(4) Firm Age		58.8	64.8	4	246
(5) Firm Size		24,357	37,534	10	122,000
(6) Cumulative		473	237	5	918
(7) Drug Novelty		-2.2	1.5	-5.3	0
(8) R&D Alliance	16				

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
(1) Incumbent	1							
(2) Diversifying	-0.32	1						
(3) Targeted Large Molecule	-0.32	-0.06	1					
(4) Firm Age	0.44	0.33	-0.36	1				
(5) Firm Size	0.65	0.13	-0.39	0.82	1			
(6) Cumulative	-0.31	0.15	0.01	-0.19	-0.21	1		
(7) Drug Novelty	0.11	0.08	-0.25	0.07	0.10	0.24	1	
(8) R&D Alliance	-0.03	-0.04	0.06	-0.07	-0.06	-0.09	-0.03	1

**TABLE 6.4**  
**Preclinical Drug Design and Clinical Trial Execution**  
**Cox Model Analysis of Drug Approval (353 Spells, 7 Events)**  
*Only Targeted Small Molecules*  
All Coefficients in *Hazard Rates*

	Model 1	Model 2	Model 3	Model 4
Incumbent	1.70 (1.31)	3.73 (4.26)	4.31~ (4.68)	5.60 (8.10)
Diversifying		3.60 (4.01)	3.00 (3.87)	4.07 (5.80)
Firm Age				0.99 (0.01)
Firm Size				1.00 (0.00)
Cumulative Introduction			1.00 (0.00)	1.00 (0.00)
Drug Novelty			1.43 (0.47)	1.38 (0.49)
R&D Alliance			0.00 (0.00)	0.00 (0.00)
Log Likelihood	-29	-28	-27.7	-27.6

~ marginal, + p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

**TABLE 6.5**  
**Preclinical Drug Design and Clinical Trial Execution**  
**Cox Model Analysis of Drug Approval (638 Spells, 15 Events)**  
*Only Targeted Large Molecules*  
All Coefficients in *Hazard Rates*

	Model 1	Model 2	Model 3	Model 4
Incumbent	1.64 (1.68)	3.05 (3.34)	2.26 (2.37)	2.29 (3.13)
Diversifying		3.91* (2.22)	4.01* (2.50)	4.70* (3.11)
Firm Age				0.99 (0.01)
Firm Size				1.00 (0.00)
Cumulative Introduction			0.99 (0.00)	0.99 (0.00)
Drug Novelty			1.27+ (0.16)	1.26+ (0.15)
R&D Alliance			2.69 (2.96)	2.63 (2.97)
Log Likelihood	-67	-64	-62.8	-62.5

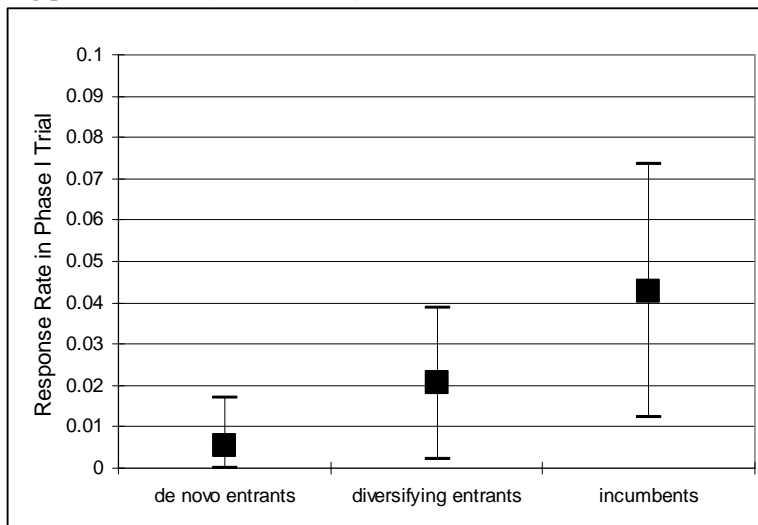
~ marginal, + p < 0.1, \* p < .05, \*\* p < .01, \*\*\* p < .001 Standard errors in parentheses.

Although the samples are becoming too small to support statistical significance, all the coefficients are of the expected sign. For those targeted anti-cancer drugs for which the manufacturing processes have not changed through the biotechnology revolution (i.e., small-molecule drugs), the result from Chapter Five holds: incumbents seem as competent as diversifying entrants in the preclinical and clinical research (note that in Table 6.4 the coefficients for incumbents and diversifying entrants are positive). The picture is different for those targeted anti-cancer drugs for which the manufacturing processes do change: large-molecule drugs. For those, diversifying entrants have an advantage in the process design, and this advantage is reflected as well in their preclinical and clinical competence (in Table 6.5, the coefficient for diversifying entrants is significant and larger than that of incumbents and of de novo firms, the baseline).

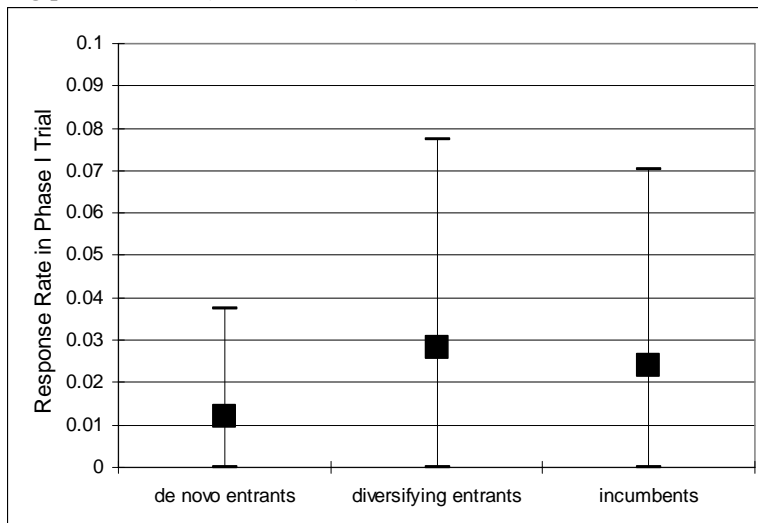
The sample to assess preclinical competence alone is rather small when stratified for targeted drugs only ( $n = 58$ ), and when further stratified as small- vs. large-molecule drugs it becomes too small for statistical analysis ( $n = 34$  and  $24$  respectively) given the size of the effects. Figure 6.1 therefore presents only a qualitative picture, without controls, of the competence for preclinical drug design, with targeted small-molecule drugs in panel 6.1a and targeted large-molecule drugs in panel 6.1b.

**FIGURE 6.1**  
**Differences in Means in Competence in Preclinical Drug Design**  
**(95% Confidence Interval)**

**(6.1a).** Mean response rates from *targeted small-molecule* anti-cancer drug phase I trials (N = 34 trials).



**(6.1b).** Mean response rates from *targeted large-molecule* anti-cancer drug phase I trials (N = 24 trials).



Again, Figure 6.1 suggests that incumbents are better at developing targeted anti-cancer drugs that are small molecules, yet diversifying entrants tend to outperform in those that are large molecules, even for preclinical drug design. The

question becomes, where does the competitive advantage in large-molecule research and development (preclinical, clinical and process) come from for diversifying entrants?

## 6.2 The Birth of Large-Molecule Manufacturing Technology

To date, biotechnology has been characterized as generating technological advances on two fronts: the methods for drug design and the manufacturing systems to mass-produce drugs (Henderson, Orsenigo and Pisano, 1998). In Chapter Four, I argued that both of these advances were disrupting the market for anti-cancer drugs and giving rise to its transition from cytotoxic to targeted drug development, a transition that officially started in 1983 with the use of Schering-Plough's *Intron A*® in cancer treatment. Furthermore, I reported that interviewees described the disruption in specific detail: whereas the availability of new drug discovery tools was advancing anti-cancer drug development from cytotoxic to targeted mechanisms of action (e.g., into mechanisms such as tyrosine kinase or angiogenesis inhibition), the availability of process innovations made the mass-production of larger molecules feasible for the first time (refer to Figure 4.4). For instance, interferon alfa-2a, the active ingredient in *Intron A*®, is a cytokine naturally produced in the human body in small quantities (Walsh, 2003) that only now can be produced in therapeutically and hence commercially feasible amounts. It is in this sense that the transition from cytotoxic to targeted anti-cancer drug development includes two sub-categories: targeted small-molecule and targeted large-molecule drugs.<sup>60</sup> It is precisely the emergence of the technology to mass-produce large-molecule drugs,

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<sup>60</sup> The reference to molecule size is literal, with interviewees describing the difference in molecular weights between large-molecule and small-molecule drugs as being approximately 10:1.



rDNA/fermentation technology, that later enabled the development of more complex large molecules in further markets. This evolution explains then diversifying entrants' lead in this particular area of research and development of targeted anti-cancer drugs.

Innovations in the rDNA/fermentation technology process were first developed to mass-produce proteins (i.e., large-molecule drugs) occurring naturally in the human body. The characterization of such proteins had been performed in academic research and was publicly available. Several of the first large-molecule drugs to reach the market were used in the treatment of enzyme deficiencies (e.g., diabetes mellitus, Goucher's disease), diseases in which not only the protein but also its therapeutic value (i.e., its connection to disease treatment) were common knowledge in the scientific community. In those markets, firms were therefore competing in terms of competence in process design alone.

Such is the case of insulin, the first product for which the radically new rDNA/fermentation technology processes were commercially used. Insulin's principal therapeutic value is the treatment of diabetes mellitus, a disease in which patients lack natural insulin production. The enzyme received the name "insulin" in 1909, but it was not until 1921-1922 that researchers at the University of Toronto isolated the enzyme and proved its effect in regulating sugar metabolism (Rosenfeld, 2002). By the time Genentech invested in rDNA/fermentation technology process innovations for mass-production of "artificial" insulin to be commercialized by Eli Lilly and Co. (Christensen, 1996), the enzyme had been in commercial production by semi-synthetic processes since 1923 (when Eli Lilly and Co. achieved successful yield and standardization of the first mass-production method).

It was not until later, as rDNA/fermentation technology evolved, that gradually other known enzymes for which no connection to disease treatment was known began to be researched in-depth. Such is the case of erythropoietin, commonly referred to as Epo, an enzyme today commercially available as Amgen's best-selling large-molecule drug for anemia treatment, *Epogen*<sup>®</sup>. According to scientist J.W. Fisher's (1998) own account of his and others' breakthrough research in "the quest for erythropoietin," one of the most important academic papers confirming the existence of Epo was published in 1950, yet

"until the gene for Epo was cloned by Lin et al. [1985] at Amgen and Jacobs et al. [1985], Epo was [erroneously] thought to be produced in the glomerular epithelial cells. The ability to clone made it possible [to determine Epo's appropriate source and therapeutic value]" (p. 10).

As the rDNA/fermentation technology processes developed, the therapeutic potential of large-molecule drugs grew in relevance and ultimately a new product class emerged. Currently, large-molecule drugs that enter clinical trials go beyond those naturally occurring in the human body, to include as well laboratory-designed drugs. Clearly, the development of the latter requires investment in terms of both manufacturing process and product design.

Interviewees described this historical progression of the research and development of large-molecule drugs: from a class of known proteins with known connections to disease treatment (e.g., insulin), to a class of known proteins with unknown connections to disease treatment (e.g., Epo), to a newly born class of engineered proteins (e.g., the new targeted anti-cancer large-molecule drug

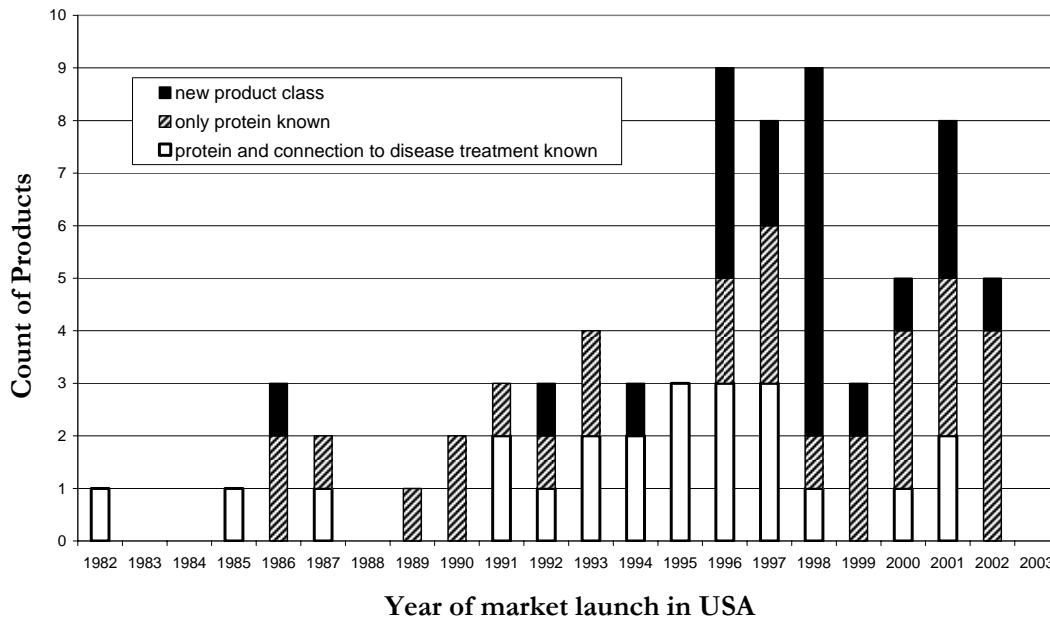
*Herceptin*®). In fact, interviewees classified large-molecule drugs currently available in the market into the three categories mentioned above (see Table 6.6).

**TABLE 6.6**  
**Classes of Large-Molecule Drugs**  
**that Evolved Chronologically into a New Product Class**

First large-molecule drugs protein and connection to disease known	Next large-molecule drugs only protein known	Newest large-molecule drugs new product class
Insulin	Epo	Monoclonal-Antibody-based products
Factor VIII	Interferons	
Human Growth Hormone	Interleukins	
Glucocerebrosidase		

Based on this classification and the list of all large-molecule drugs approved in the USA up to 2003 as reported in Walsh (2003), I constructed Figure 6.2 to illustrate the emergence of the new product class over time.

**FIGURE 6.2**  
**The Emergence of Large-Molecule Drugs as a New Product Class**



Based on Figure 6.2, I generate a list of firms that first participated in rDNA/fermentation technology and for whom, that lead translated later into a competitive advantage in targeted large-molecule drugs in the anti-cancer drug market (see Table 6.7).

**TABLE 6.7**  
**Pioneer rDNA/fermentation Technology Process Innovators**  
**and their later Firm Profile in the Market for Anti-Cancer Drugs**

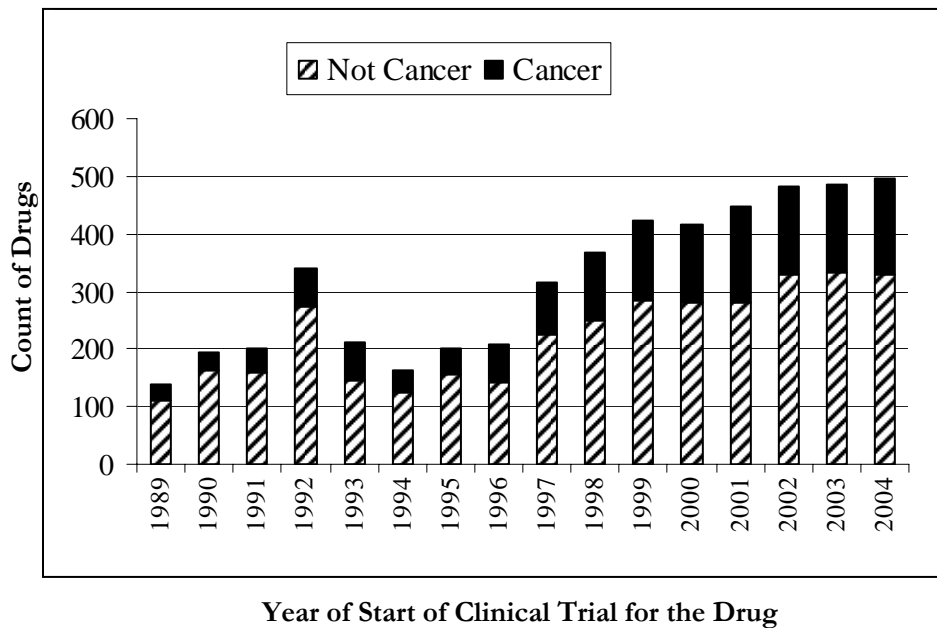
Year (Approval in USA)*	Brand Name	Commercializing Firm	Original Developer	Firm Profile of Original Developer when Competing in Targeted Anti-Cancer Drugs
1982	Humulin	Eli Lilly	Genentech	Diversifying entrant
1985	Protropin	Genentech	Genentech	Diversifying entrant
1986	Intron A	Schering Plough	Schering Plough	Diversifying entrant
1986	Roferon A	Hoffman-La Roche	Hoffman-La Roche / Genentech	Incumbent / Diversifying entrant
1986	Orthoclone OKT3	Ortho Biotech (Johnson & Johnson)	Ortho Biotech (Johnson & Johnson)	Diversifying entrant
1987	Activase	Genentech	Genentech	Diversifying entrant
1987	Humatrope	Eli Lilly	Eli Lilly	Incumbent
1989	Epogen	Amgen	Amgen	Diversifying entrant
1990	Procrit	Ortho Biotech (Johnson & Johnson)	Ortho Biotech (Johnson & Johnson)	Diversifying entrant
1990	Actimmune	Genentech	Genentech	Diversifying entrant
1991	Novolin	Novo Nordisk	Novo Nordisk	Other
1991	Leukine	Immunex (Amgen)	Amgen	Diversifying entrant
1991	Neupogen	Amgen	Amgen	Diversifying entrant
1992	Recombinate	Baxter / Wyeth	Baxter / Wyeth	Diversifying entrant / Incumbent
1992	Proleukin	Chiron	Chiron	Diversifying entrant
1992	OncoScint CR/OV	Cytogen	Cytogen	De Novo entrant

\* All years according to Walsh (2003) seem systematically lagged compared to appearance in the *Physician Desk Reference*.

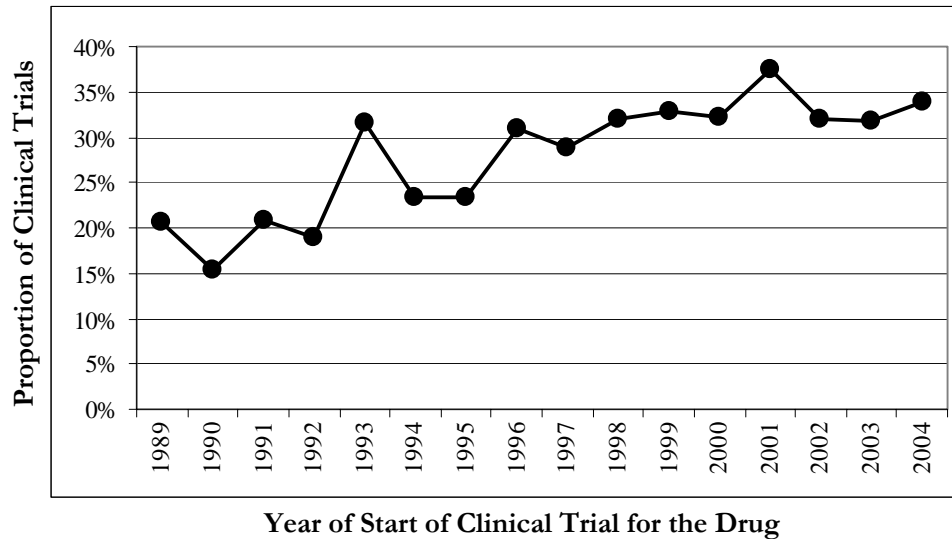
Furthermore, I repeat the exercise based on drugs in clinical trials. Using *Pharmaprojects* as the source, I identified the 33,257 drugs that entered clinical trials in

the period 1989-2004 for any indication. After discarding 10,769 drugs (32% of the total) for which no description is available in the database to classify the drug as a large- or small-molecule drug, I identified 5,474 drugs as large-molecule drugs. After discarding 351 of those drugs (6% of all large-molecule drugs) because they lack information on their dates of introduction, I ended with a sample of 5,123 large-molecule drugs that entered clinical trials in the period 1989-2004 for any indication. I then classified them as anti-cancer or not (there is not enough information for direct classification per the three categories presented in Table 6.6). The resulting pattern is shown in Figure 6.3 whereas the increasing proportion of large-molecule drugs in clinical trials dedicated to cancer treatment is shown in Figure 6.4.

**FIGURE 6.3**  
**Increasing Presence of Large-Molecule Drugs in Clinical Trials,**  
**And among them, of those for Cancer Treatment**



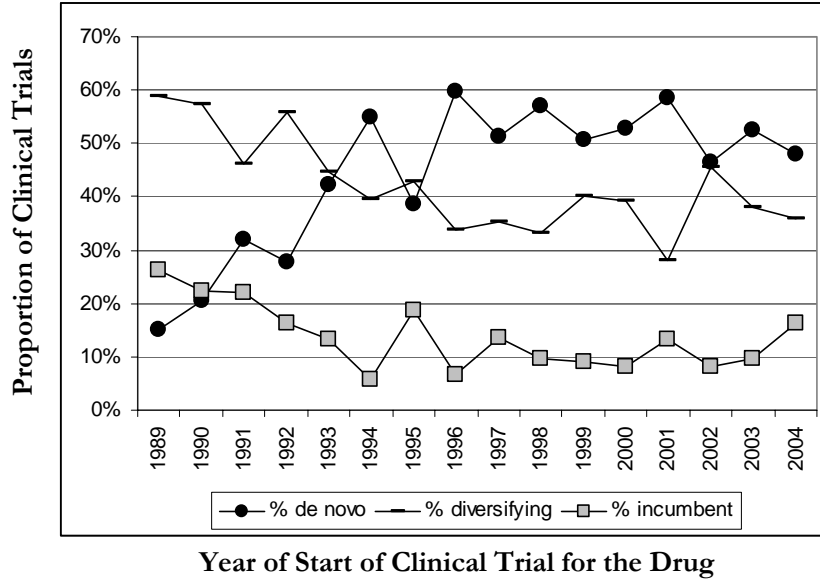
**FIGURE 6.4**  
**Increasing Proportion of Large-Molecule Drugs in Clinical Trials**  
**Dedicated to Cancer Treatment**



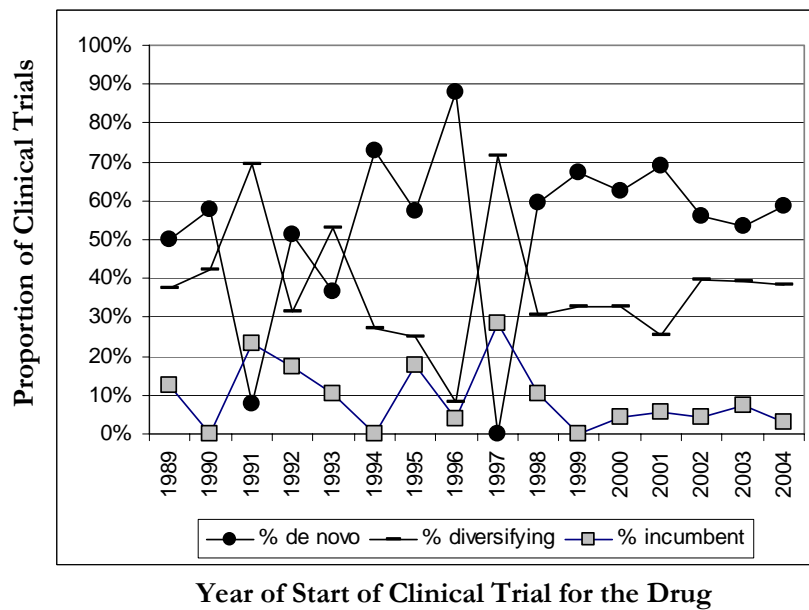
In Figure 6.5, I take the fraction of large-molecule drugs that are generated by firms involved in the anti-cancer drug market (even if the drug is not for cancer treatment), and separate them by the profile the firm adopts in this market. The pattern in Figure 6.5 shows how diversifying entrants were initially the major producers, although in later years, de novo firms have surpassed them.

Finally, in Figure 6.6, I repeat the same exercise but restricted to large-molecule drugs that specifically target cancer treatment. Again, anti-cancer market incumbents are the least present firm category.

**FIGURE 6.5**  
**Proportion of Large-Molecule Drugs in Clinical Trials**  
**Generated by Each of the Three Populations of Firms**  
**Competing in the Anti-Cancer Drug Market**



**FIGURE 6.6**  
**Proportion of Anti-Cancer Large-Molecule Drugs in Clinical Trials**  
**Generated by Each of the Three Populations of Firms**  
**Competing in the Anti-Cancer Drug Market**



## 6.3 Discussion

### 6.3.1 Resource Bases, First Movership and Competitive Advantage

I have presented in this chapter the case of the competences in process design in this market in two steps. First, I showed the differences across the three firm categories, and their links to differences in the other two competences, preclinical and clinical. Secondly, I traced the birth and evolution of those process design competences to find where diversifying entrants' competitive advantage in large-molecule production came from. This case under study joins then the literature on the origins of competitive advantages and sheds some additional light on the topic.

In their classic review of first-mover advantages and disadvantages, Lieberman and Montgomery (1988) raised the question of whether the criterion of “first-movership” was into a market or into an R&D area (p. 51). Ten years later, in the update to their classic review (Lieberman and Montgomery, 1998), the authors stated their original proposition more clearly for strategy scholars: “We believe that the greatest opportunities may lie in forging links with the... resource-based view of the firm...” (p. 1111).

It is precisely this link that I extend in the present chapter. Although the literature on first-mover advantages refers to first movers into a market, the resource-based view of the firm has clearly stated the dual and orthogonal existence of markets and resource bases. In his classic piece, Wernerfelt (1984) proposed to look at firm activity as a product-resource matrix (reproduced previously in Chapter Five, Figure 5.5). In this matrix, markets (i.e., sets of substitutable products, to which the author referred to simply as “products”) span several resource bases for



product development. Likewise, the same resource base could be utilized to develop products for several different markets.

In the case of large-molecule process design, a set of firms moved into various markets through moving first into a unique and emerging resource base: rDNA/fermentation technology. Genentech did so to enter the market for insulin, Amgen to enter the market for anemia treatment, and Genzyme to supply for the first time to the latent market for glucocerebrosidase, to name a few. As the technology, that is, the resource base, evolved, those firms started diversifying into the more profitable anti-cancer drug market, a classic resource-base-induced diversification strategy (Montgomery and Hariharan, 1991). The case I present in this chapter therefore shows how being first to move into a *resource base* later translated into a competitive advantage in a different market.

This case joins a recent stream of research focused on the birth of capabilities (see Helfat and Lieberman, 2002, for a review of the topic). Ahuja and Katila (2004) used a sample of all firms in the chemical industry in the period 1979-1992 to show how the evolution of firms' capabilities is not only path-dependent, but the heterogeneity in capabilities is highly firm-idiosyncratic. In a study of the Software Services Industry in India, Ethiraj, et al., (2005) presented an analysis of inter-project heterogeneity in one firm to discuss as well the heterogeneous evolution of central capabilities in this industry.

In the case study in this chapter, I extend this recent work by moving further from measuring the evolutionary nature of competence formation, and tracing two additional components: the birth of the resource base, and its use in achieving a competitive advantage when diversifying into a different market. In doing this, I

bypass the main critiques of former work in this line of research (Ethiraj et al., 2005). In-depth historical accounts of single-firm cases (e.g., Iansiti and Khanna, 1995; Rosenbloom, 2000) have been criticized for not showing the competitive advantage generated, measurable only in comparative analysis in a large-sample study. On the other hand, large-sample studies (e.g., Silverman, 1999) have been criticized for not choosing data fine grained enough to measure a single resource base. By combining data on inter-firm comparison in the market for anti-cancer drugs with the evolution of a single resource base, rDNA/fermentation technology, I offer here the first attempt in this literature to address both ends of the spectrum of critique.

### 6.3.2 Assembled vs. Nonassembled Product Markets

Beyond the value of moving past first-movership into markets, and into first-movership into resource bases that translate later into competitive advantage in a specific market, the nature of this case as a study of competence in process innovations generates further insight.

Process innovations, that is, the design of manufacturing processes to mass-produce products, have always been recognized as key elements of a firm's survival and even competitive advantage (e.g., Clark, 1996). Most commonly, process innovations are discussed as product innovations' complements within a firm's R&D function.<sup>61</sup>

For radical technological changes, the classic model of industry dynamics introduced by Abernathy and Utterback (1978) is widely used to understand the

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<sup>61</sup> Outside of R&D, the appropriate and reliable implementation of process innovations in manufacturing installed capacity has, in fact, been described as independent of product innovations, as an important mediating factor between the successful completion of R&D and the appropriation of rents (that is, as a complementary asset for commercialization [Teece, 1986]).

interface between product and process innovations. The authors explained how, after a radical technological change disrupts a market, experimentation in terms of product features is pursued by all firms, both incumbents and entrants. When customers finally settle on a dominant design for the product (i.e., a set of specific product features), firms without “access” to the dominant design are forced to leave the market, and a smaller set of firms stays to compete (Utterback, 1994; Christensen, Suarez and Utterback, 1999). The dynamics of competition then gradually shift from “product differentiation” (i.e., competing in terms of the innovative quality of products) to “price differentiation” (i.e., competing in terms of price reductions for a set of rather standardized products). Driven by these dynamics, innovation across firms gradually shifts from product innovation (the source of innovative quality in the product) to process innovation (the source of cost reduction in the mass-production of the product). Process innovations become then the center of attention for firms’ investment until another wave of creative destruction shocks the market.

Beyond Abernathy and Utterback’s (1978) classic study and the discussion of process innovations within the context of radical technological change, a long tradition of research has given particular attention to innovation that, although beyond incremental, is not entirely radical (Brown and Eisenhardt, 1997). Because such innovations offer a combination of strategic value and a seemingly higher frequency of appearance throughout the life of a firm, they represent an important set for analysis (Hayes, Wheelwright, and Clark, 1988, p.273-278). This line of research has been extensive. In one area of it (frequently informed by the operations research tradition) attention to process innovations has been given mainly with the

objective to coordinate product and process innovation functions within the corporate R&D apparatus of firms (e.g., Ha and Porteus, 1995; Krishnan, Eppinger and Whitney, 1997). Another area in this line of research is frequently referred to as operations or manufacturing strategy. Scholars in this group have sought to understand the strategic investments that a firm can make in terms of selection of new products and their accompanying new processes, given the firm's knowledge of the current structure of its entire production system (Hayes, Wheelwright and Clark, 1988; Hayes and Pisano, 1996).

Much less attention has been paid, however, to the contrast between markets characterized by intensive investment in product innovation and those characterized by intensive investment in process innovation. To my knowledge, this contrast has been referred to as the discussion of assembled vs. nonassembled product markets,<sup>62</sup> and only two main discussions in the area are widely recognized.

One is Tushman and Rosenkopf (1992) where the authors argued that nonassembled product markets, being less complex in technology, actually involve less complex sociopolitical dynamics during technological change. The other is Utterback (1994). The author explains that, although the original model in Abernathy and Utterback (1978) extends from assembled to nonassembled product markets, there are distinctions in the contrast. The latter in fact have shorter periods of product experimentation, and hence competition moves into price differentiation (and hence process experimentation) much earlier. When we consider how many markets within the global economy fit the description of "nonassembled," that is, as

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<sup>62</sup> However, the term "nonassembled" has been recognized as an oversimplification in the current literature. Utterback (1994) clarifies that "...these product 'classes' [assembled vs. nonassembled] are neither inclusive nor easily defined" (p. 123). I prefer the distinction of product-innovation vs. process-innovation intensity.

*process-* rather than *product-*innovation intensive, the amount of research available to advise managers in those settings in strategy formulation seems rather limited. For example, within the pharmaceutical industry alone, it is estimated that 25% of all products required primarily a process innovation for development, since the product is of natural occurrence (Walsh, 2003). Even though some studies exist on radical innovation in nonassembled markets (e.g., Peck, 1961, studied innovations in aluminum extraction; Enos, 1962, petroleum extraction; and Tang, 1988, steel extraction), further research is required.

#### **6.4 Limitations**

The main limitations of the study in this chapter are the same as those in Chapter Five: the research is based on a revolution that is still unfolding, and hence results only hold “up to this point” in the competition. It is, nonetheless, significantly informative to document the case of the birth of a competence that evolved into a competitive advantage for diversification into a major market, even if that competitive advantage is not sustained throughout the revolution.

#### **6.5 Conclusions**

The present case shows how diversifying entrants into the anti-cancer drug market achieved a competitive advantage in a sub-set of the new technology: targeted large-molecule drugs. They did so by moving first into an emerging resource base used for other markets and that was later re-used for their diversification attempt to move into anti-cancer drugs. Beyond increasing our understanding of first-mover advantages and their connection to the resource-base view of the firm for the case of

diversifying entrants, this case gives further attention to the competitive scenario faced by incumbents.

Prior work emphasized the separation of underinvestment and incompetence as determinants of incumbents' failure in the face of radical innovation (Henderson, 1993). In Chapters Four and Five, I discussed the question of incompetence and its sources in theory and empirical analyses, respectively. The question of first-mover advantages and in general, of order of entry, brings attention back to investment timing. In the present study, I found no difference across firm categories in start of investment into the overall new technology. The only difference I found was in the sub-set of large-molecule drugs. Beyond the question of how diversifying entrants achieved a competitive advantage in targeted large-molecule anti-cancer drug development, the question of the case of incumbents remains. Why didn't they invest earlier in targeted large-molecule anti-cancer drug development, so they would be first-movers into the emerging resource base as well?

A classic in this line of research is Christensen's (1997) discussion of how new technologies many times underperform in the main dimension of merit for the incumbents' market, and only over time evolve to compete against the incumbents' products, with the additional advantage of unexpected ancillary features.

The case at hand shows a different path, and in doing so constitutes an "empirical irregularity." Dimensions of merit in the focal market (i.e., that of anti-cancer drugs) have not changed in unexpected ways. All market participants have known that the main dimensions of merit in anti-cancer drug development are efficacy and safety both in the cytotoxic period and throughout the current biotechnology revolution.

Indeed, the present case study redirects the main research question away from the characterization of the evolution path for the new technology (whether it comes from niche markets, underperforming in the incumbents' main market, and/or with unexpected ancillary features) as Christensen's (1997) pioneering research stated. The present case study reshapes the research question into the broader query: "[whether it is] difficult for an incumbent to perceive the threat and take adequate preventative steps" (Lieberman and Montgomery, 1988, p. 48). In creative destruction, the central dynamics are those of adaptation vs. replacement of incumbents. Therefore, a central question during the period of environmental change (in the case of creative destruction, a change in technology) should be whether incumbents can recognize the change as a threat in time to begin adaptation (and/or preemption). The crucial constraint is precisely the fact that "organizational decision makers also face constraints on the information they receive" (Hannan and Freeman, 1989, p. 67; see also the discussion of Arrow [1974] in that text). The main task at hand is not only to characterize the evolutionary path that a competing new technology follows. It is rather to understand how the emergence of a competing new technology (through a large set of evolutionary paths) is sometimes not recognized as a threat by market incumbents until it is too late, and then to find solutions in terms of organizational strategy and alternative structure. Research in this line, specifically in the inertia in the ability of firms to monitor their changing environment through information flows, is emerging. In a pioneering article on this topic, Williams and Mitchell (2004) document a study of information infrastructure (through which firms monitor their changing environment) and the likelihood of diversification into specific markets for the eight largest telephone service providers

in the US in the period 1984-1998. Although pioneering, the article highlights the key difficulty that investigating this topic will present: the distinction between inertia and rational choice. In other words, based on current research it is impossible to tell current research impossible to tell whether firms choose their diversification attempts due to biased information (the firm collected information through an inertial information infrastructure) or to rational choice under full information (the firm collected full information and chose to diversify into areas related to its current business).<sup>63</sup> Although challenging in measurement, this area certainly holds a significant promise for research in strategy in periods of environmental change.

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<sup>63</sup> The issue becomes more salient in Williams and Mitchell (2004) as the level of bias in information infrastructure between the diversifying firm and the potential market for entry was measured through four elements of the organizational domain: customer, product, function, and location. These are exactly the same elements that Haveman (1992) used to measure relatedness of diversification (with the exception of “location” whose variance Haveman [1992] did not have to measure because her setting, the Savings and Loan Industry in California, was one region).



## Chapter 7

# Conclusions

I started the present dissertation by narrowing down my interest to the R&D of products under an emerging new technology during a period of “creative destruction.” I then chose as an empirical setting the market for anti-cancer drugs based, among other criteria, on its extreme research intensity. I set out to study biotechnology’s impact on this market, and hence to measure differences in research competences across categories of firms as the market transitioned from cytotoxic to targeted drug development.

In the end, four main points consumed my attention:<sup>64</sup> (1) the pervasive confusion present in the literature between incumbents vs. entrants and established vs. de novo firms, that is, between market incumbency and organizational experience; (2) the three large sets of mechanisms at play during a period of technological change (namely, competence re-use, inertia and new competence development); (3) the proposition that R&D competences might be decomposable into a technology-specific and an application-specific side, and the strategic implications of this separation; and (4) the proposition that if markets and resource bases are equally relevant parts of the life of a firm, then competitive dynamics such as first-mover advantages should apply equally to markets and resource bases.

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<sup>64</sup> I offer in-depth discussions of findings and conclusions derived in Chapters Five (sections 5.4-5.6) and Six (sections 6.3-6.5).

## 7.1 Market Incumbency and Organizational Experience

As discussed in Chapter Three, market incumbency and organizational experience are two distinct and orthogonal constructs. Market incumbency refers to the presence of a firm in a market at the time this market is disrupted by an unfolding technological change. A firm can be either an incumbent or an entrant with respect to a specific market. Organizational experience, in contrast, is a process by which an organization remains in operation, becoming ever more efficient (and also more engrained) in its current business(es). A firm can be established or de novo regardless of the market in question. In that sense the distinction mirrors two levels of analysis present in mainstream strategy: business-unit (i.e., market) and corporate (e.g., Rumelt, 1991).

Market incumbency is a construct defined by market (i.e., at the business level). The same firm can therefore be an incumbent in one market and an entrant in another. IBM, for example, was an incumbent in the tabulator market as this market transitioned from mechanical to electrical tabulators, but a diversifying entrant in the typewriter market as this market transitioned from mechanical to electrical typewriters (Utterback, 1994; Yates, 2005).

Organizational experience is a construct defined by firm (i.e., at the corporate level). Regardless of the market(s) in which a firm operates, the firm is either established or de novo. Incorporated in 1911,<sup>65</sup> IBM had been in operation as a firm for decades by the time it faced the “electrification revolution.” IBM was thus an established firm in competition in both the tabulator and the typewriter markets during their transitions.

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<sup>65</sup> According to the IBM Archives available at [http://www-03.ibm.com/ibm/history/history/decade\\_1880.html](http://www-03.ibm.com/ibm/history/history/decade_1880.html)

Decoupling the two constructs of market incumbency and organizational experience requires then three instead of two firm categories: incumbent firms (incumbent, established), diversifying firms (entrant, established) and de novo firms (entrant, de novo).

The loose use of the terms “incumbent” and “established” as interchangeable terms has led our understanding of creative destruction to several misconceptions that only under the light of more recent research have become noticeable. One is the point that motivated the present study: the conclusion that only incumbents would incur organizational inertia and hence research incompetence. But others can be identified. The literature contains cases where evidence from diversifying entrants or from established firms in general is used to understand incumbent dynamics.

Even our underlying theoretical models have incurred a penalty. For example, in reviewing the dynamics of cannibalization, Conner (1998) explains how previous literature has highlighted the fact that when the incumbent invests in the new technology, its profits are  $B - A$ , where  $B$  is the new profit and  $A$  is the loss of the previous business profit stream. In contrast, the entrant’s profits are simply  $B$ . Obviously, entrants have better incentives to innovate. Yet if both incumbents and diversifying entrants are coming from prior operations, the model should be elaborated. For incumbents, the loss might be less than  $A$  if the old technology business gets to run in parallel for a period of time, and if some of it gets to be re-used, lowering the cost of developing the new technology. For diversifying entrants, the profits should be  $B - A$ , since sometimes the diversification attempt is meant to facilitate exiting the previous business (Helfat and Eisenhart, 2004). Further, even when no exit is considered, the diversification attempt may be made even though

there is some probability that the firm might incur a loss in its base business during the attempt (Mitchell and Singh, 1993). Only de novo firms have B as a profit stream if successful because they have no previous operation to jeopardize. But since de novo firms have no competences to re-use from prior operations either, their costs might also be higher.<sup>66</sup> This brings us beyond the separation of incumbents and established firms, and into the underlying dynamics by firm category.

## 7.2 Competences: Good, Bad and Gone

In light of the three firm categories proposed, I then reviewed the mechanisms present during a period of technological change to summarize three sets: competence re-use, inertia and new competence development.

Competence re-use is the “good.” In some areas of R&D, the technological change leaves previously acquired competences undestroyed. These competences represent an advantage for established firms during the period of technological change.

New competence development is (strictly speaking, replaces) the “gone.” In some areas of R&D, the technological change destroys the value of competences. These competences are gone, and in those areas established and de novo firms start from scratch and compete on equal ground (unless any other mechanism is present, such as differential access to university research or to patented innovations).

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<sup>66</sup> Notice that the original models reviewed by Conner (1998) had equal costs for both incumbents and entrants. Incumbents' profits were  $B - A - C$  and entrants' were  $B - C$ , and therefore,  $C$ , the cost, dropped out of the comparative analysis. If the three categories of firms are considered, and if re-use of prior competences reduces the costs, then cost considerations must re-enter the equation. Incumbents' profits are then  $B - A_i - C_i$ , diversifying entrants' are  $B - A_d - C_d$ , and de novo entrants' are  $B - C_n$ . Only in the comparisons of losses ( $A$ 's) and costs ( $C$ 's) does the competition unravel.

Lastly, inertia is the “bad.” It is not so straightforward for established firms to recognize competences that have been destroyed by the technological change. If established firms fail to discard competences that are no longer of value and instead attempt to re-use them, they incur a disadvantage, the liability of inertia.

Competence re-use and inertia only accrue to established firms since they stem from prior experience. Unless there is a reason to believe otherwise (e.g., differences in investment level or timing, or differences in the type of technological change the disruption represents for incumbents vs. diversifying entrants), these two sets of mechanisms will bring incumbents and diversifying entrants closer to each other in R&D performance and further away from de novo firms, as was the case in the present study.

I moved then to pay additional attention to the dynamics of competence re-use. I did so in this study by searching for relevant sub-categories.

### **7.3 Technology-Specific and Application-Specific R&D Competences**

After seeing that incumbent firms were leading in performance even in the area of R&D where these firms’ competences were fully destroyed, I proposed that R&D competences might be decomposable into an application-specific and a technology-specific side. By the start of a disruption, the application-specific side of R&D competence has accrued only to incumbents and could represent a unique source of competitive advantage for these firms even in areas of R&D where the technology-specific side of R&D competence is fully destroyed.

Within this perspective, the number of competences available for re-use to incumbents increases. Incumbents can re-use all competences in areas of R&D left

undisrupted, and can also re-use application-specific competences in areas of R&D where technology-specific competences are fully destroyed.

Indeed, the definitions that the original work offered for related diversification are worth reviewing:<sup>67</sup>

“Entry into new product-markets based on the firm’s existing resources [diversifying entrants]. Introduction of new products in a firm’s existing market [incumbents].” (Penrose, 1959 p. 110).

“Businesses are related to one another when a common skill, resource [diversifying entrant], market [incumbent] or purpose applies to each.” (Rumelt, 1974 p. 29).

Certainly, they seem to encompass both incumbents and diversifying entrants.

By giving recognition to the true strengths of incumbent firms, I hope to move forward in pinning down their true weaknesses, and hence, the true sources of their underperformance.

By offering a longitudinal perspective of the phenomenon, I also hope to advance toward reconciling the resource-based (e.g., Wernerfelt, 1984) and evolutionary (e.g., Hannan and Freeman, 1984) views of competition. Montgomery (1993) highlights the differences in these views by pointing out the contrast of how routines and resources are viewed as sources of inimitability and hence advantage in the resource-based view, yet as sources of inertia and hence disadvantage in evolutionary perspectives. It is precisely because routines and resources, and their resulting competences, support stability that they are two sides of the same coin.

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<sup>67</sup> These two definitions in particular are cited in Helfat and Eisenhardt (2004, p. 1218) in opening their discussion of intra-temporal vs. inter-temporal economies of scope.

When the environment is stable, routines and resources promote stability and hence are good for the firm. When the environment changes, routines and resources *still* promote stability. In areas left undisrupted, such stability is an advantage, but in areas disrupted by change, stability is a disadvantage, it obstructs strategically planned change (Hannan and Freeman, 1984). For a firm, the value of routines and resources (and resulting competences) derives from the firm's relationship with its environment, and this relationship evolves over time. It is only in a longitudinal view that the evolution of such a relationship, and hence, of the value of different bundles of routines and resources can be captured.

Combining a longitudinal perspective with the resource-based view, I moved then to my last point: first-mover advantages.

#### **7.4 First-Mover Advantages and the Market-Resource Matrix**

Lastly, I came back to the discussion of the dual presence of product-markets and resource bases in the life of a firm (e.g., Wernerfelt, 1984). Recognizing that both elements are of equal value for the firm's activity, I then proposed that both elements should receive equal importance in our theories of competition. Specifically, I suggested expanding our interest from the advantages that accrue to first movers into a market, into the advantages that accrue to first movers into a resource base.

In the end, in my opinion, a crucial aspect in the current state of the Strategy field (and thus of Technology Strategy as a sub-field) is precisely the agenda set forth by Porter (1991): to move past the "cross-sectional" interest and into the

“longitudinal” endeavor in our discussion of competition and competitive advantage. If this is done, the currently distant resource-based and evolutionary views (Montgomery, 1993) will inevitably come closer together. After all, for those of us interested in competition in periods of technological change, there seems to be no way to live with one view, without the other.



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